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Neuropsychological differentiation of children and adults with and without non-psychotic, unipolar major depressive disorder.

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Neuropsychological Differentiation of Children and Adults With and Without Non-Psychotic, Unipolar Major Depressive Disorder

by

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Abstract

The current investigation was conducted to see if it would be possible to differentiate groups of participants with and without depression based on data from a comprehensive neuropsychological assessment. The first goal was to apply cluster analytic algorithms to the neuropsychological data for participants with and without depression. This was conducted in separate procedures for the child and adult groups. The second goal was to examine the internal validity of the groups, using multiple clustering algorithms. The third goal was to examine if internally valid solutions represented groups or subgroups that were comprised by a large majority of participants with a diagnosis of depression.

Participants in the study were two hundred and ninety-four clients referred by neurologists, in the greater Indianapolis, Indiana area, to an independent clinic for neuropsychological evaluation. Cluster analyses utilizing neuropsychological data yielded reliable and technically valid cluster solutions for both the child and adult data. The child and adult cluster solutions were characterized by performance level across most subtests of the neuropsychological battery, with a greater division of performance levels present in the adult cluster solutions. Both the child and adult solutions were comprised of clusters that did not differ significantly with respect to a diagnosis of depression. Therefore, the technically valid cluster analyses utilized in the current investigation, conducted on data from a comprehensive neuropsychological evaluation, dif not differentiate, in a statistically significant way, participants with and without a diagnosis of depression in both the child and adult groups. Additional cluster analyses conducted with only sensorimotor data identified cluster solutions that were characterized by unique

patterns of finger tapping performance and grip strength. Both child and adult solutions in the additional analyses were not comprised of clusters that differed significantly regarding a diagnosis of depression. Thus, the technically valid solutions from the additional analyses in the current investigation, conducted on sensorimotor data, also did not differentiate, in a statistically significant way, participants with and without a diagnosis of depression in both the child and adult groups. The implications, limitations, and future research considerations arising from the current investigation were discussed.

To my classmates, now colleagues, Erin Warriner and Annmarie McCullen, I thank you very much for the support and companionship over the years. Finally, of greatest importance, I would like to acknowledge the tremendous support I have received from my family. My mother, Rita Ahmad, has encouraged, supported, assisted, and inspired me to persevere. It is the many beautiful qualities in her, that I admire and strive to attain, that helped me continue my educational pursuits. For my father Imtiaz Ahmad, his genius, perspective, support, and knowledge continue to guide me along a path of human development that allow me to achieve my goals. I am glad that along the way he has taken up Psychology as a hobby. To my husband, Bilal Itani, whose selfless support of my education and career has given me peace and strength, I am forever deeply appreciative. Finally, for my children, my son Muhammad who inspires and energizes me with his beautiful spirit and my daughter, Amatullah, whose memory I hold dear in my heart, I am thankful.

Table of Contents

List of Tables

List of Figures

Chapter I: Introduction

Neuropsychologists focus on brain-behavior relationships. The specific behavioral conditions upon which neuropsychological efforts are focused, in both clinical and research settings, are increasing in number. Analyses and evaluations taken from a neuropsychological vantage point are frequently requested by a wide range of specialists including neurologists, psychiatrists, general practitioners, and special educators. In parallel, the research efforts conducted in these areas of specialization have served to underscore the importance of a close examination of the brain-behavior relationships in many conditions—depression is one such condition.

Depression as a Brain-Based Disorder: A Brief History

The general notion that mental illness is related to brain dysfunction and that depression represents a unique form of mental illness are longstanding. Early in the understanding of depression it was not distinguished from other forms of mental illness. In the 1900s, Emil Kraepelin developed a classification of depression that distinguished it from schizophrenia and further recognized that it could alternate with periods of elevated mood (Fox, 2002). Over the years, the brain-behavior relationship attributed to depression has driven many conventional treatments for this disorder. Freud had taken a brain-behavior approach to his understanding of depression (Gupta, Kumar, & Kasper, 2002).

Pharmacological and other treatments for depression, although frequently found by chance to be successful, have served to contribute to the continued focus of the brain-behavior relationships in depression over the years. Electroconvulsive

therapy used in the 1950s to treat depression that had otherwise been refractory is one example of the acceptance of these sorts of treatments. Also in the 1950s, by chance, Iproniazid, an antitubercular drug was noted to cause an elevation of mood and increase in activity level (McAllister-Williams, Ferrier, & Young, 1998). This drug was later identified as acting to block the activity of monoamine oxidase, an enzyme that destroys the monoamine neurotransmitters norepinephrine, serotonin, and dopamine in synapses that extend the duration of the active status of these neurotransmitters in the brain.

Shortly thereafter, Imipramine, the first of the tricyclic anti-depressants was the impetus for the next popular wave of anti-depressant treatments. These anti-depressants work by blocking the re-uptake of norepinepherine and serotonin so that they also remain active in the synapse for a longer amount of time. Thus, by the end of the 1950s two major waves of anti-depressant therapies had served to stimulate a climate of focus on neurotransmitters as the key to conventional pharmacological treatments (Videbech et al., 2003).

In the early 1980s, the mechanisms of pharmacological intervention became more specific, thereby reducing the broad side-effects of antidepressants. Selective serotonin reuptake inhibitors (SSRIs) became popular in this regard because they inhibited the reuptake of serotonin thus allowing for fewer side effects and a comparatively quick action. The trend for the treatment of depression with pharmacological agents that act to regulate specific neurotransmitters continues to be the focus of primary treatment for depression in many settings, including most

recently antidepressant drugs that include dopamine reuptake inhibitors and alpha-2 receptor antagonists. Their specificity makes them particularly popular because of the decreased side effects (Stuss & Levine, 2002; Videbech et al., 2003).

In the discipline of neuropsychology, prior to the mid 1970s, there was predominant support for the notion that depression was related only to very minor neuropsychological deficits (Friedman, 1964). However, in the mid 1970s (initiated by the review of Miller, 1975), there was increased interest in viewing depression from a neuropsychological vantage point.

Initially, research took the form of thorough case studies (e.g., Cavenar, Maltbie, & Austin, 1979). Over the years, group studies were conducted. However, as Veiel (1997) points out in his review, series of investigations examining neuropsychological characteristics of depression conducted in a systematic manner have been rare in comparison to other areas of research in neuropsychology and allied disciplines. As a result, a clear consensus as to the precise nature of neuropsychological characteristics related to depression, if any, has yet to emerge.

Whereas conventional notions of depression include, within their broad framework, suspect dysfunctional brain systems, research has yet to provide clear, consistent results to support any particular brain-based model in this regard. Indeed, there are no structural lesions correlated with common depressive experience and this poses a problem for traditional or simplistic approaches to establishing brain-behavior relationships.

A review of neuropsychological research efforts conducted over the past few years indicates many reasons for this lack of clarity. First, many studies have been conducted on a very limited sampling of behaviors. This has served to impede thorough analyses of relative deficiencies of depressed persons and has limited the generalizability of results to known brain-based systems of complex behavior. Research in the areas of decision-making, attention, memory, and psychomotor speed are examples in this regard. Results in any one area do not provide adequate information about the relative assets and deficits that would be expected to arise from a thorough neuropsychological evaluation.

A second limitation of recent research efforts in the area of depression is that many studies are conducted examining neuropsychological deficits of persons with depression who are otherwise normal in their behavioral functioning. It is frequently difficult to interpret these results because such normative controls often involve volunteers or recruits who do not share important demographic and other characteristics with the participants who are depressed. Often, differences are found between groups with and without depression (i.e., "normal" volunteers) that are the result of above average normative control group functioning as opposed to deficient functioning in groups with depression (e.g., Schatzberg et al., 2000). Finally, results are frequently questioned as to whether they are due to the unique depressive experience or other confounding factors (e.g., the higher than average IQ of a group of university volunteers). Furthermore, the ecological validity of these results is

limited, given the complexity of comorbid dysfunction that is usually seen in the neuropsychology clinic.

A third limitation represents the other end of the research spectrum. There has been a trend, over recent years, in neuropsychologically based research efforts, to investigate the characteristics of depression within the context of specific brain damage or brain-based diseases/disorders. Examples of some of the more common efforts in this regard include, but are not limited to, Parkinson's disease (e.g., Youngjohn, Beck, Jogerst, & Caine, 1992), Human Immunodeficiency Virus (e.g., Harker et al. 1995; Rourke, Halman, & Bassel, 1999), Huntington's Disease (e.g., Nehl, Ready, Hamilton, & Paulsen , 2001), Chronic Obstructive Polmunary Disease (e.g., Yohannes, Baldwin, & Connoly, 2000), stroke (e.g., Hosking, Marsh, & Friedman 2000), and Traumatic brain injury (e.g., Sherman, Strauss, Slick, & Spellacy, 2000).

In both research and clinical settings, depressive symptoms can result in the overestimation of the severity and frequency of the neuropsychological deficits of these disorders/diseases. However, these research efforts are very useful for understanding the specific characteristics of depression manifest within the context of such disorders. However, their results are difficult to extrapolate to depression, in general. Indeed, meta-analytic investigations are limited by drastically differing methodological frameworks and thus fall short of speaking to general brain-behavior system inefficiencies in depression. However, if depression is manifest uniquely within the context of each disease process, this sort of research is very useful.

A fourth limitation to the current body of depression research is that much of the knowledge of neuropsychological characteristics of depression does not take into account possible unique factors related to age and any enduring characteristics across the agespan. Much of the literature in the child- and older adult- based research is limited to extrapolation of findings for young- and middle- aged adults. Results from such a research investigation that may examine one or both of these areas would allow for the identification of possible homogeneous subtypes of persons with depression. It would also allow for previous research investigations to clarify the relation between age and the neuropsychological characteristics of depression. This is important because this relation is currently unclear.

What has not been attempted is to differentiate groups based on data from a comprehensive neuropsychological assessment across different age ranges.

The current investigation is an attempt to conduct such a research investigation. In an effort to provide a context for the rationale, goals, and any predictions of the current investigation, a review of conventional notions of depression, and data that underscore its importance in clinical settings, is presented.

Second, a review of recent findings regarding neuropsychological characteristics of depression is discussed (i.e. the "behavior" in the "brain-behavior" relationship). Third, discussions of unique child findings followed by unique older adult findings are presented. Next, a discussion of recent findings in brain-based research (i.e., the "brain" in "brain-behavior") is presented. Finally, a brief discussion of special methodological considerations in neuropsychologically-based

depression research is discussed and leads to the rationale and goals for the current investigation.

Conventional Notions of Depression

Conventional notions of depression involve persistent depressed mood, loss of interest and pleasure and, for persons 18 years or younger, usually involve abnormal irritable mood (American Psychiatric Association, 2000). Persons who are depressed also usually experience a number of accompanying symptoms including appetite or weight disturbance, sleep disturbance, loss of energy or fatigue, self-reproach or inappropriate guilt, poor concentration or indecisiveness, and/or thoughts of death or suicide.

The Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV; American Psychiatric Association, 1994), and most recently, the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition Text Revision (DSM-IV-TR; American Psychiatric Association, 2000) are commonly used reference manuals that both clinicians (e.g., psychiatrists, neurologists) referring clients for neurological assessment and researchers utilize to conceptualize and diagnose persons with depression.

There are many qualifiers for a variety of depressive experiences (e.g., recurrent, chronic, mild, moderate, severe, etc.) however the essence of depression is characterized by the presence of a Major Depressive Episode. Table 1 presents the DSM-IV-TR criteria for a Major Depressive Episode.

The focus of the current discussion is on Major Depressive Disorder (APA, 1994) as defined by the DSM (e.g., DSM-IV,1994; DSM-IV-TR, 2000), that is referred to throughout the current discussion, for convenience, as *depression*. The reason for utilizing this particular classification of depression is that it is currently the most commonly used conceptualization of depression in clinical and research efforts.

According to DSM classification criteria, persons with major depressive disorder are characterized by a history of one or more depressive episodes (see Table 1) in the absence of a history of manic episode and wherein the depressive episode(s) is (are) not due to the direct effects of a substance or general medical condition. The depressive episode(s) also must not be better accounted for by a related psychotic disorder.

There is evidence to suggest that these distinctions are important from a neuropsychological standpoint and that depression together with a history of manic episode has a unique set of neuropsychological characteristics (e.g., Martinez et al., 2000) as does depression occurring within the context of psychosis (e.g., Aguglia, DeVanna, Onor, & Ferrara, 2002; Schatzberg et al. 2000).

Estimates of lifetime prevalence of Major Depressive Disorder range from 10% to 25% in women to approximately 5% to 12% in men (American Psychiatric Association, 2000; Steffen et al., 2000). It is estimated that approximately 5% of persons 19 or older are afflicted with depression in any given year. Of note,

Table 1

DSM-IV-TR Diagnostic Criteria for Major

Depressive Episode

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest of interest or pleasure.

Note: Do not include symptoms that are clearly due to a general medical condition, or mood-incongruent delusions or hallucinations.

(1) depressed mood most of the day, nearly every day, as indicated either by subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful). **Note:** In children and adolescents, can be irritable mood.

(2) markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others)

(3) significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. **Note:** In children, consider failure to make expected weight gains.

(4) insomnia or hypersomnia nearly every day

(5) Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)

(6) Fatigue or loss of energy nearly every day

(7) Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)

(8) Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others)

(9) Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

B. The symptoms do not meet criteria for a Mixed Episode.

C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

E. The symptoms are not better accounted for by Bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

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particularly to neuropsychologists, is the statistic that approximately 25% of persons with general medical conditions (e.g., stroke, carcinomas, diabetes) are expected to develop Major Depressive Disorder during the course of their illnesses (American Psychiatric Association, 2000).

Conventional notions of depression in children remain to be debated in both scientific research and clinical settings. Some have argued against the existence of depression in children. However, recently DSM-IV diagnoses of Major Depressive Disorder rendered for children in clinical settings have increased. Point prevalence estimates vary widely and range from .2% to 4% percent of pre-teen school-age children (e.g., Ball, Rice, & Thapar, 2000; Birmaher et al. 1996; Cicchetti & Toth, 1998). Recent studies have shown that in pre-teen children prevalence estimates occur equally in males and females. Because depression in children is a relatively newly accepted condition, point prevalence statistics likely represent underestimates of the actual prevalence of this affective disorder.

Approximately 2.3% to 8% percent of teenagers and adolescents have been diagnosed with depression at any given time (e.g. Cicchetti & Toth, 1998; Harrington, 1994) according to DSM-IV criteria. Of concern, recent investigations also indicate that 70% to 80% of depressed teenagers do not receive treatment (Keller, Lavori, Beardslee, Wunder & Ryan, 1991; Rohde, Lewinsohn, & Seeley, 1991) and 20% to 50% of depressed teenagers have a high comorbidity of substance abuse, conduct disorder, and other mental disorders. Male to female ratios of depression in adolescence and teenage years are approximately the same as found for adults,

whereas male to female ratios for children are approximately equal (Ball, Rice, & Thapar, 2000).

Depression has its highest prevalence in the older adult population (usually considered as beginning at age 60-65). Approximately 15% to 25% of elderly persons are experiencing depressive symptoms at any point in time, with recent estimates indicating up to 15% of persons over 65 years of age have a formal depressive-spectrum diagnosis at any given time. Depression can be particularly troubling in the elderly and has been found to be related to worse perceived health and greater bodily pain when compared to non-depressed older adults (Judd et al., 2000; Vandenberg, Oldehinkel, Brilman, Bouhuys, & Ormel, 2000). As with the non-elderly adults, there are a greater proportion of females diagnosed with depression in older adults (Beekman, Copeland, & Prince, 1999; Palsson & Skoog, 1997), however precise estimates for this statistic vary widely.

Despite recent debates pertaining to the accuracy of prevalence, incidence, and presentation across age groups, depression represents the most common mental disorder diagnosis (40-50 percent of diagnoses) across all clinical settings and therefore is quite worthy of study.

Neuropsychological Characteristics Related to Depression

A wide variety of neuropsychological deficits have been identified in studies examining groups of depressed persons. Research findings have resulted in the implication of nearly all aspects of neuropsychological functioning in one study or another. Results from some extensive meta-analytic and original research

investigations suggest that neuropsychological functioning in persons with depression is similar to that of persons with global-diffuse impairment in brain functioning (e.g., Reischies & Neu, 2000, Veiel, 1997). When excluding studies that have not been replicated and/or have significantly questionable methodological or analytical flaws, there remain some general trends evident for deficiencies in specific neuropsychological domains. A discussion of the domains that have been actively examined is presented.

Attention.

In a recent meta-analysis of the neuropsychological deficits associated with depression, Veiel (1997) examined all studies published between 1975 and 1995 and found that in the area of attention and concentration, the only measures that were used consistently enough as attention measures to include in his analysis were the Digit Span subtest of the Wechler scales (Wechsler, 1981; Wechsler, 1987) and an analogous visual Block Span task (Richards & Ruff, 1989). Using fairly stringent methodological exclusionary criteria for his meta-analytic design, based on the results of three studies and an adjusted total N of 200, he found no substantial differences between depressed groups and normal controls in attention functions as measured by these tests, with only 2.8% of the average proportion of depressed participants scoring two standard deviations below the normal mean.

More recently, Grant, Thase, & Sweeny (2001) examined the Trail Making Test part A (Reitan, 1969), Digit Span (Wechsler, 1987), and the Continuous Performance Test (Conners et al., 1995) performance for 123 unipolar, non-psychotic

adult patients with a DSM-IV diagnosis of depression in a sample mixed for other psychiatric history and 36 normal controls. As with Veiel (1997), they found no significant differences between the group of depressed participants and the group of control participants on these tests of attention.

These findings exemplify results found in similar recent studies comparing depressed and non-depressed groups on commonly used measures of attention (e.g., Ilsley, Moffoot, & O'Carroll, 1995). Despite these findings, attention continues to be considered by some as a suspect deficiency in persons with depression. This may be due to isolated research findings for specific aspects of attention (e.g., Williams et al., 2000). Some of these findings have occurred within the context of specific sample characteristics such as when studying inpatient participants or groups of participants diagnosed with depression and psychosis, however others have occurred when studying outpatient participants diagnosed with unipolar, non-psychotic depression (e.g., Landro, Stiles,& Sletvold, 2001).

Schatzberg et al. (2000) found that depressed participants with psychosis (N=11) evidenced significant deficiencies when compared to non-psychotic depressed participants (N=32) and normal controls (N=23) on the Stroop task colour naming portion and the colour-word portion, with effect sizes greater than 1.00. Although both of the depressed groups (psychotic and non-psychotic) obtained significantly relatively deficient interference scores than did comparison participants, these relative deficiencies were within the normative average range, with normal comparison

participants performing well above average. Results on the Trail Making Test part A in this study did not yield any significant differences between the groups.

Basso, Lowery, Neel, Purdie, & Bornstein (2002) have found significant deficiencies in performance on the Trail Making Test part A in a group of non-psychotic, depressed participants when compared to normative controls, however the depressed group also met criteria for bipolar disorder and was from a larger inpatient population.

Attention deficiencies for participant groups with depression that were neither inpatient nor compared to groups functioning above average have also been found. For example, Landro et al. (2001) used stringent selection criteria, including diagnoses based upon the viewing of structured clinical interview by two independent, experienced clinicians with kappa=0.84 for agreement, controlling for medications, and selecting non-hospitalized outpatients with unipolar, non-psychotic major depressive disorder. Overall there were 22 participants in the depressed group and 30 normal controls in the non-depressed group; there were no statistically significant differences between the two groups for age, education, or intelligence estimate ($p>.05$). Findings on the selective attention task of the Automated Psychological Test was significantly lower for the group of participants diagnosed with depression.

Therefore, there is no clear-cut evidence that attention difficulties are an inherent neuropsychological characteristic related to depression, although they have

been shown to be present under specific participant subtypes and in some more general studies.

Memory.

Results from many memory studies have been shown to identify significantly poorer memory functioning in persons with depression in comparison to control participants without a diagnosis of depression. However, not all aspects of memory have been shown as deficient in these groups and an equally sizeable number of studies have found *no* specific deficiencies in groups of participants with depression.

In their meta-analytic investigation, reviewing 99 studies between the late 1960s and 1992, Burt, Zembar, & Niederehe (1995) examined patterns of memory impairment related to depression. Their selection criteria for samples were fairly stringent, considering inpatient versus outpatient status, subtypes of persons with depression (e.g., bipolar disorder, with psychosis), and whether participants were receiving pharmacological intervention. However, their selection criteria for measures were quite liberal, grouping all verbal memory tests into either verbal recall or recognition (immediate and delayed) and visual memory tests into either visual recall or recognition (immediate and delayed) as opposed to conducting analyses for specific tests (e.g., California Verbal Learning Test). Using these criteria, there were 71 studies analyzed for the verbal memory procedures and five studies analyzed for the visual memory procedures.

Results have been found demonstrating significantly poorer performance ($p < .05$) for groups with depression versus normal controls (functioning in the average

range) on verbal and visual recall and recognition. However, analyses of specific group findings did not support significant differences in this regard for outpatient groups, rather results supported significant differences for inpatient, unmedicated, and bipolar participant groups versus normal controls.

Since Burt, Zembar, & Niederehe's (1995) meta-analysis, a number of studies have been conducted further investigating recall versus recognition in persons with depression. Findings have been mixed regarding support for significant deficiencies in memory function for persons with depression versus controls.

Ilsley, Moffoot, and O'Carroll (1995) examined performance on the Rivermead Behavioral Memory Test for a group of 15 inpatient participants with depression and an age, IQ, sex, and handedness control group. They found significant ($p < .05$) deficits on the verbal and visual recall but not verbal and visual recognition portions of the Rivermead Behavioral Memory Test. These findings occurred despite intact performance on measures of attention (e.g., Digit Span). These authors proposed that an interpretation of these findings could be taken to indicate specific retrieval deficits related to depression, that are not due to attentional or motivational difficulties.

The results of Isley, Moffoot, & Carroll (1995) have been supported by the work of other authors (e.g., Fossati, Deweer, Raoux, & Allilaire, 1995) whose results have shown deficient recall versus recognition on verbal and visual tasks for persons with depression in comparison to control groups. However, conclusions directly implicating retrieval are not necessarily the only explanation for these findings.

Organization of information and initiation are two processes that have recently come into question when interpreting findings of impaired free recall for persons with depression. There is a paucity of research investigation findings that clarify the precise processes contributing to deficient impaired free recall in groups of persons with depression (e.g., Channon, Baker, & Robertson, 1993). Furthermore, given the more general lack of consistent support for the presence of any deficient memory processes for depressed persons, there is insufficient evidence to confidently suggest any relationship in this regard.

Executive functioning.

There has been considerable recent attention given to possible deficiencies in "executive functions." Although there is no clear agreement as to precisely what constitutes executive functions in all studies, the functions that have been most actively investigated are briefly reviewed.

Verbal fluency is one area that is commonly considered as an executive function. There have been a number of recent research investigations designed to explore verbal fluency functioning in groups of persons with depression. Findings quite consistently support significant verbal fluency deficits for groups of outpatient participants diagnosed with unipolar, non-psychotic depression when compared with either outpatient participants who are non-depressed or normal, recruited control participants. A brief presentation of some of the more recent studies in this regard is presented.

The aforementioned investigation conducted by Landro et al. (2001) using stringent selection criteria also explored verbal fluency performance for 22 participants in a non-psychotic, unipolar, outpatient depressed group and 30 normal controls in the non-depressed group, with groups equated for age, education, and psychometric intelligence. The Controlled Oral Word Association Test (Spreen & Benton, 1969) F-A-S form was used as a measure of verbal fluency. A significant difference was found ($p<.01$) between total number of words generated for the depressed and non-depressed groups, with the depressed groups generating a significantly fewer number of words when raw scores were corrected for sex, age, and education.

Grant, Thase, & Sweeny (2001) also examined performance on the Controlled Oral Word Association Test in for 123 unipolar, non-psychotic adult patients with a DSM-IV diagnosis of depression in a sample mixed for other psychiatric history and 36 normal controls. However, in their investigation, differences between the depressed and non-depressed groups for total number of responses on this measure were non-significant ($p>.05$).

The above mentioned two examples are representative of the overall mixed results for performance on verbal fluency measures with participants diagnosed with depression. When examining many studies using the Controlled Oral Word Association Test, in his meta-analysis, Veiel (1997) found that the average difference, based on 3 studies, with an adjusted total N of 118, was 0.55 standard deviations. Only 11% of depressed participants scored in the deficient range (i.e., 2 standard

deviations below the mean). Thus, the burden of establishing clear-cut deficiencies related to depression remains.

A second area frequently cited as deficient in persons with depression is the area of mental flexibility (also described using other descriptors such as "set shifting"). By far, the most commonly, and almost exclusively, utilized test in research investigations examining mental flexibility is the Trail Making Test, Part B or some variation of this test. Time taken to complete the test is usually utilized, however some investigators utilize the difference between normative performance on the time taken to complete Trail Making Test, Part B and the normative performance on the time taken to complete the Trail Making Test part A. Findings examining performance on the Trail Making Test part B represent some of the most robust significant differences between depressed and non-depressed groups in the area of the neuropsychology of depression.

Veiel's (1997) meta-analysis examined all studies published between 1975 and 1995 related to the neuropsychological functioning of depression. He included three studies with an adjusted total N of 108 to examine mental flexibility as determined by performance on the Trail Making Test, Part B. He found that the average standard difference between the depressed participant groups and non-depressed participant controls was two, with 50.2 % of depressed participants falling at least 2.0 standard deviations below the means for time taken to complete this test.

Veiel (1997) proposed that these results reflected considerably and consistently impaired performance of depressed participants on this measure. There

have been many other studies published since Veiel's (1997) meta analysis that support these findings.

Landro et al. (2001) compared the normative performance on the Trail Making Test part B with the Trail Making Test part A for 22 outpatient participants with unipolar depression and 30 healthy controls. They proposed that by utilizing this comparative statistic (i.e., part B versus part A) they would control for baseline motor performance and increase sensitivity to mental flexibility (i.e., shifting from numbers to letters). Performance in the group of participants diagnosed with depression was significantly deficient ($p<.05$) for the part B performance.

Despite these findings there are a smaller number of studies that have not found significant deficiencies for on the Trail Making Test part B. Grant, Thase, and Sweeny (2001) did not find significant differences for this test when studying unmedicated depressed outpatients. However, average Wechsler IQ in their sample was somewhat higher than in other studies (107.9 for depressed participants and 107.1 for control participants). Thus, although there is not 100% consensus of findings indicating deficiencies in the area of mental flexibility, it appears reasonable to assert that results of most studies with stringent selection criteria and sound methodological designs identify deficiencies in this area.

A third area of executive functioning from among the more common areas investigated is that of concept formation and hypothesis testing. This area of executive functioning is less frequently investigated than the aforementioned areas of verbal fluency and mental flexibility. Concept formation and hypothesis testing are

frequently absent from major reviews, meta-analytic investigations, and larger data analytic studies (e.g., Basso & Bornstein, 1999; Landro et al., 2001; Veiel, 1997).

The majority of research investigations that have examined concept formation and hypothesis testing have utilized the Wisconsin Card Sorting Task (Berg, 1948) as a measure in this area, whereas a much smaller number of studies have used the Category Test (Reitan & Davison, 1974) usually on specific populations (e.g., persons with traumatic brain injury).

Because of the relative fewer number of investigations in the areas of concept formation and hypothesis testing, research investigations are often limited to specific populations and results regarding concept formation and hypotheses testing, as they relate to general notions of depression are limited.

Ilonen et al. (2000) examined Wisconsin Card Sorting Test Performance in a group of 29 persons diagnosed with nonpsychotic depression (most of whom were inpatient status at the time of the assessment) and 30 recruited controls from general hospital and university populations. Significant differences ($p<.05$) were found for total number of categories completed, total number of trials, total number of errors, perseverative errors, non-perseverative errors, and percent conceptual level responses. Full-Scale IQ from the Wechsler Adult Intelligence Scale-Revised (WAIS-R; 1981) was approximately equal in the samples. The authors proposed that the lower percentage of conceptual level responses and the higher number of perseverative errors (despite feedback) was indicative of impaired concept formation.

At first blush, it may appear that the inpatient status of the participants in the Ilonen et al (2000) research investigation might been a confounding factor contributing to presence of significant findings. In a similar study, Ravnkilde et al. (2002) also examined the performance on the Wisconsin Card Sorting Test in a group of 40 severely depressed hospitalized inpatients and 49 controls matched for age, gender, years of education, and socioeconomic status. Results did not represent significant (p <.05) differences for total number of trials, categories completed, trials to complete first category, total number of errors, perseverative errors, conceptual level responses, failure to maintain set, or learning to learn.

Merriam et al. (1999) assert that given the convergence of executive deficits with neuroimaging studies indicating resting-state and activation deficits in persons with depression, it is surprising that studies utilizing executive tests fail to find support for deficiencies in executive functioning. They propose that inclusion of participants at different phases of their illness, administration of medications, and discrepant IQ and education between depressed and control groups are the only plausible explanations for this absence of significant findings. To support their argument, they examined the performance on the Wisconsin Card Sorting Test for 79 outpatient participants with depression who were tested prior to any initiation of treatment at the beginning of the course of their illness. They compared their performance to 61 healthy control participants who were matched for age and Wechsler IQ. In contrast to the findings of Martin, Oren, & Boone (1991) and Raviknlde et al. (2002), significant differences between groups were found for the

number of categories, learning to learn, nonperseverative errors, perseverative errors, perseverative responses, percent of conceptual responses, and items to first category. The only non-significant difference was the failure to maintain set score.

Despite discrepant findings reviewed above, there is some agreement indicating that performance on the Wisconsin Card Sorting Test is deficient. However, much less clear is the interpretation of these findings. Whereas some aspects of this test are clearly related to concept formation, there are a number of other processes also involved in task requirements. For example, the frequent finding that failure to maintain set on the Wisconsin Card Sorting Test is not significantly different for participants with depression could be taken to support the aforementioned findings of Grant Thase, and Sweeney (2001) and Veiel (1997) that attention is not deficient in persons with depression. Further exploration into the additional processes that could be implicated and concurrent investigation into the relative functioning of multiple brain processes may assist with clarification of seemingly inconsistent results.

Visual-spatial-organization.

Also commonly examined, but with less frequency, are deficits in visual-spatial organization related to depression. Although visual-spatial-organizational abilities are frequently required in many tasks included in a broad range of domains, there are a wide variety of tasks used in studies examining visual-spatial-organizational abilities, including Block Design and Object Assembly subtests of the Wechsler Scales (e.g., Weschler, 1981) and the copy trial of the complex figure

memory tasks (e.g., Osterreith, 1944). Findings in this area are mixed, and do not currently support any clear relationship between deficiencies in visual-spatial-organization and depression.

Veiel (1997) included the copy trial of the Rey Complex Figure test and the Block Design and Object Assembly subtests of the Wechsler scales in his meta-analysis. Three studies with an adjusted total N of 180 met inclusion criteria for analysis of visual-spatial functions. The average standard difference was minimal for the Block Design and Object Assembly subtests (i.e., less than 0.87 standard deviations from the mean). Although the average standard deviation was somewhat larger (1.62) on the Rey Complex Figure copy trial. However, it appeared the results were due to a small cluster of data at the low end of the range, with only 15% of results falling in the deficient range (i.e., at least 2 standard deviations below the mean).

More recently, Schatzberg et al., 2000 examined Weschler Block Design performance for 32 outpatients with depression and 23 normal controls. There were no significant differences ($p>.05$) on Block Design performance between the outpatient and control participant groups.

In contrast, Landro et al (2001), found significant differences in visual-spatial-organizational functioning. They examined performance on the Weschler Block Design subtest for 22 outpatient participants with unipolar depression and 30 healthy controls. Results indicated significantly ($p<.05$) worse performance for the group of

outpatient participants in comparison with the control group that was functioning approximately at the normative average.

Persons who argue that visual-spatial-organizational deficits are not significantly related to depression cite the influence of motor speed and coordination as confounding variables on the abovementioned tests of visual-spatial-organization. Indeed, these variables have been suspect as deficient in persons with depression, most notably motor speed. Until replication of these studies occurs within the context of a larger sampling of neuropsychological functions such as those suspected to confound results, clarification on this matter may not occur.

Psychomotor Functioning.

A review of the literature in the area of psychomotor functioning indicates that imprecise tests, the problem of interrater agreement, and other methodological factors may serve to contribute to the paucity of valid and reliable results to review. Despite this paucity, motor activity has long been suspected as dysfunctional in persons with depression. Kraepelin had implicated voluntary movements as "the most obvious clinical features" of the disease (Kraepelin, 1904). In their review of the psychomotor symptoms of depression, Sobin and Sackeim (1997) assert that objectively measured gross motor functioning, fine motor functioning, motor aspects of speech, and motor speed, have been shown to reliably differentiate persons who are depressed from other psychiatric and normal comparison groups.

Motor speed is one example of an observed behavior and reported symptom for persons with depression although as with most motor functions, in comparison to

many other aspects of neuropsychological functioning, such as memory and executive functioning, there have been fewer research investigations examining the motor characteristics of depression. Research investigations designed to examine motor deficits in persons with depression were initially designed to examine simple manual motor speed. Findings were inconsistent in this regard, with some providing support for slowed motor speed, bilaterally, some studies providing support for left-handed slowed motor speed (in right-hand-dominant persons), and other studies indicating no differences in motor speed (e.g., Rohling, Greene, Allen, & Iverson, 2002).

As the focus of research investigations in the area of the motor characteristics related to depression has become more refined and specific there have been some clear trends to explain these differences. Many investigators in this area have come to agree that any research design conducted in this area must control for reaction time (considered a pre-frontal function related to initiation and planning).

Rogers et al. (2000) demonstrated this sort of approach in their study of the motor characteristics in 23 participants with depression and 24 age-matched controls. Their independent experimental paradigm was designed to measure speed of motor movement, controlling for reaction, under both internally and externally cued conditions. Their findings supported a significant slowing of motor movement during reaction to a stimulus under conditions requiring internal cueing. They compared these findings to studies showing deficiencies with motor speed under internally cued conditions in groups of persons with Parkinson's disease. Moreover, because the motor signs of depression respond well to pharmacological treatment, they and others

with similar findings propose that dysfunction is not purely structural in nature, but possibly due to a disruption of dopaminergic input to the prefrontal cortex.

Other less often examined motor deficiencies related to depression are the differences in motor aspects of speech, most notably articulation (e.g., Kuny & Stassen, 1993; Nilsonee, 1988). In general, experts in the areas of speech and language consider motor characteristics related to depression as having great potential as indicators of response to treatment and some propose that the identification of psychomotor retardation may be the most consistently predictive indicator of good response to tricyclic antidepressants (Joyce & Paykel, 1989). However, there is currently insufficient evidence to confidently support this notion.

There are many research investigations that have neglected the importance of motor symptoms. Reasons often discussed include a lack of objective measures in addition to the potential subjectivity of traditional motor examinations. Thus, in their recent review of the psychomotor symptoms of depression, Sobin and Sackeim (1997) characterize the current knowledge of psychomotor symptoms related to depression as "conceptually obscure" despite a large body of evidence supporting their significant presence.

Neuropsychology of Depression in Children.

It is only a recent phenomenon that widespread acceptance has occurred for the view that depression in children exists as a similar experience to that for depression in adults. Because depression in children is a relatively newly accepted condition, the study of it is far less developed in the literature than for adults. The

foundations for acceptance of depression as a childhood disorder similar to that of adults have proliferated because of recent positive remission of symptoms found in some children diagnosed with depression when treated with similar pharmacological agents that provide symptom relief for adults. The pharmacological interventions of choice for children are currently SSRIs; this has stemmed from their ease of administration (usually once per day) and their relatively fewer noxious side effects in comparison with tricyclic antidepressants (Michael & Crowly, 2002). Double-blind, placebo controlled medication trials for tricyclics (e.g., Hazell, O'Connell, Heathcote, Robertson, & Henry, 1995) have provided little support for various pharmacological interventions above and beyond the effects of placebo. However, recent research efforts have shown the benefit of SSRIs over placebo on measures of affect, global improvement, and remission of depressive symptoms in adolescents 12 to 19 years of age (Emslie et al., 1997).

In the late 1980s, there began an examination of isolated cognitive functions children with depression (e.g., Kinsbourne, 1987). Over the past 15 years there have been very few research investigations examining the neuropsychological characteristics of children with depression. The most widely examined neuropsychological domain is that of learning and memory in children with depression. Among the research investigations conducted, findings have been similar to the adult literature, yielding no clear-cut evidence to suggest that depression in childhood and adolescence is significantly related to learning and memory (e.g., Horan, Pogge, Borgaro, Stokes, & Harvey, 1997). By far, the most comprehensive

study conducted on the neuropsychological functioning of children with depression was by Livingston, Stark, Haak, & Jennings (1996). Livingston et al., (1996) who examined the performance of 17 children with unipolar depression (average age of 13 years, 8 months) on the full Halstead-Reitan Neuropsychological Battery for Children. Means and standard deviations were plotted. There was no one area or test that fell below one standard deviation below the mean in comparison to normative data. The lowest area of performance, a Freedom From Distractability composite composed of the average of Arithmetic, Digit Span, and Digit Symbol Coding results of the Wechsler scales was calculated as a standard score of 92 (SD=10). This was reported by these authors as an area of relative deficit when compared to most other tests and domains of neuropsychological functioning for which obtained means were within a few standard points of 100 (although not tested for significant difference). Research investigations are beginning to focus on executive functions in children, however these investigations taken as a body of research are in the very early phases of exploration.

Neuropsychology of Depression in Older Adults.

In accord with findings in research investigations examining the general adult population, depression in older adulthood has been shown to be related to significant cognitive deficiencies. However, as with the child studies, there have been very few investigations examining a broad range of neuropsychological characteristics of older adults with depression. In the research investigations that have been conducted, a wide range of deficiencies have been found such as processing speed, attention,

verbal memory, visual memory, naming, reading comprehension, etc. (e.g., King et al, 1995). However, replication of research investigations have not identified clear-cut areas of deficiency have been reliably identified (Boone et al, 1995).

Of important consideration in investigations related to depression in older adulthood is the confounding effects of cognitive decline and early dementia on results. It has been frequently found that depression is present in the early stages of some forms of dementia and design of research investigations and interpretation of results is best conducted with the possible effects of dementia in mind. Despite a paucity of studies examining a full range of neuropsychological functions, there have been some studies conducted that examinined multiple neuropsychological characteristics. Boone et al., (1995) examined the neuropsychological functioning of 73 "older," healthy, unmedicated outpatient adults diagnosed with depression and 110 control participants. The average age of the participants in the depression group was 61 years and the average age of controls was 63 years. A full neuropsychological battery was administered to each patient including the WAIS-R (Wechsler, 1981), Stroop Test (Stroop, 1935), Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1978) , Rey-Osterrieth Complex Figure (Osterreith, 1944), Wechsler Memory Scale-Revised (Wechsler, 1987), Auditory Consonant Trigrams (Peterson, 1966), Wisconsin Card Sorting Test (Berg, 1968), and Controlled Oral Word Association Test-FAS (Benton & Hamsher, 1978). Participants in the depression group were also rated, according to the Hamilton-Depression Rating Scale, as either mildly or moderately depressed. Increasing severity of depression (i.e., "normal" versus

"mild" or "mild" versus "moderate") was found to be significantly associated ($p<.05$) with decreased information processing speed (Wechsler Index) and executive function performance (Wisconsin Card Sorting Test, COWAT, Stroop Test) but not for verbal or visual memory tests on the Wechsler Memory Scale. These findings are in accord with a general trend in recent research investigations that have found processing speed and executive functioning deficits in groups of older adults with depression. Furthermore, these findings appear to remain even when factoring out medications, age of onset, and symptom severity (e.g., Palsson, Johansson, Berg, & Skoog, 2000).

Of significant consideration, when studying older adults is the presence of comorbid medical illnesses. Depression prevalence rates vary, however are reported in much higher rates than with the general population for specific medical conditions (e.g. Yohannes, Baldwin, and Connolly, 2000) and can be quite high. Furthermore, some of these conditions can contribute to neuropsychological functioning and as a result should be controlled for in depressison-based research.

Brain-Based Research

Given the ambiguous findings of research on the neuropsychological characteristics of depression a brief discussion of brain-based research findings is presented. This discussion constitutes an attempt to provide further scientific information to assist with reconciliation of the neuropsychological findings across research investigations.

In a similar manner to the neuropsychology research wherein various deficits have been found related to depression, there have also been numerous findings from neuroimaging research investigations supporting possible dysfunction in numerous brain regions. The current discussion is limited to the findings for which there appears to be replication and agreement.

Whereas many traditional models of depression have had a primarily "top-down" focus in that affective state is the result of negative thinking (e.g., Beck, Rush, Shaw, & Emery, 1979), neuroimaging research investigations are frequently conducted within the framework of a "bottom-up model." These research investigation focus on how neurological dysfunction causes negative mood and further affects cognition (e.g., Liotti & Mayberg, 2001). Neurotransmitter systems, including serotonin, norepinephrine, dopamine, acetylcholine, and gamma-aminobutyric acid systems have all been implicated as related to depression. In addition, in some depressed persons hormonal disturbances such as elevated glucocorticoid secretion and blunted growth hormone, thyroid-stimulating hormone, and prolactin responses have been identified as imbalanced. To date, there is no one particular imbalance that is related to all individuals with depression. Rather, it is considered that neurochemical and neuroendocrine systems serve to influence brain systems in a dysfunctional manner creating a condition that give rise to depression. It is the brain systems that are of great interests in neuropsychological discussions.

As Liotti and Mayberg (2001) point out, the lack of a lesion upon which to focus brain-behavior research related to depression has led efforts in this regard to

focus on functional neuroimaging as a window for viewing possible suspect dysfunctional systems.

Stuss and Levine (2002) propose that the frontal lobes are involved in almost all aspects of human neuropsychology and are pivotal to the final outcome of affective experience. A review of recent neuroimaging research investigations indicates that abnormal activity in the prefrontal regions of the brain is the most common finding. Neuroimaging research investigations examining depressed persons have identified dysfunction in corticostriatal loops. There are a series of parallel corticostriatal loops that are comprised by topographical projections from the prefrontal cortex to the striatum, and indirectly through the pallidum and thalamus returning to the same areas of the prefrontal cortex (Alexander et al, 1986). Functional impairment has been found at each level of this corticostriatal loop in persons with the depression.

Positon Emission Tomography (PET) and Single Photon Emission Tomography (SPECT) research investigations have replicated findings in the area of depression. Findings demonstrate that persons with depression show deficient performance on tasks of executive functioning involving planning, inhibition of perseverative responding, internal monitoring, and concept formation (e.g. on the Tower of London planning task, Continuous Performance Task, Wisconsin Card Sorting Test). These participants fail to show augmentation of caudate nucleus, anterior cyngulate, and rostrolateral prefrontal cortex, to the same degree displayed

with normal controls (i.e. appeared hypometabolic) in both PET and SPECT research investigations(e.g., Elliott et al, 1997; Liotti & Mayberg, 2001; Merriam et al., 1999). Although there are a number of other findings indicating hypometabolism in certain brain regions during cognitive tasks related to depression, they have not been sufficiently replicated to warrant any conclusive assertions.

There are a number of models that have been developed to explain the aforementioned findings pertaining to prefrontal cortical –subcortical system dysfunction in depression. Liotti and Mayberg (2001) propose that the prefrontal regions, most notably right prefrontal cortex, are responsible for inhibiting emotional responses stimulating from limbic regions. This model accounts well for early notions that the right cerebral hemisphere is preferentially responsible for emotional control (e.g., Borod, Koff, Lorch, & Nicholas, 1986).

Most recently, models of depression have been developed that serve to account for the recent findings of both left and right frontal dysfunction in addition to more longstanding (e.g., right posterior) dysfunction. For example, Shenal, Harrison, and Demaree (2003) propose that dysfunctional left frontal activation is related to decreased positive affect, whereas dysfunctional right frontal activation is related to emotional dysregulation, and right posterior dysfunction is related to decreased arousal and impaired emotional responsiveness. This is one of many such models proposed to explain brain functioning in depression, and all are in need of further scientific investigation to substantiate their assertions.

Thus, what appears to be a reasonable, evidence-based standpoint is the view that there may quite possibly be a relation of dysfunctional frontal-subcortical systems to the neuropsychological deficits evident in persons with depression, although the precise nature of this relation remains unclear and in need of further investigation. This standpoint is consistent with some of the aforementioned neuropsychological findings related to some tasks of executive functioning. In addition, it is in accord, at the most basic level, with our knowledge of the mechanisms of action of some of the most common antidepressants and the presence of serotonin and dopamine receptor sites in the pre-frontal cortex.

The Current Investigation: Main Considerations

Results from neuropsychological and neuroimaging research investigations have yet to provide reliable and valid findings that indicate neuropsychological data can clearly differentiate persons with and without depression. Although there appears to be growing evidence that those neuropsychological characteristics thought to be subserved in large part by the prefrontal cortex are involved in depression, there have not been research investigations that have clearly shown its dysfunction uniquely accounts for depressive experience.

There are a number of considerations evident through the body of literature reviewed that are important for the current investigation and that are helpful to maintain in an attempt to identify unique groups of depression based on neuropsychological functioning.

First is the issue of the diagnosis of depression. In order to compare research related to depression with the overwhelming majority of research investigations conducted on this topic, DSM classification would appear to be an appropriate choice. Furthermore, based on the research investigations outlined earlier in the present discussion, it appears that self-rating of depressive symptoms is an unnecessary and possibly confounding method for classifying depression, adds no appreciable information to the results (i.e., as previously mentioned severity in outpatient populations has been shown not to be related to deficiency presentation or severity), and can tend to be overestimated by participants (e.g., Rohling, Green, Allen, & Iverson, 2002). Both severity of current episode (independent of hospitalization status) and number of previous episodes have no significant effects on the neuropsychological functioning in research investigations with groups of depressed persons (e.g., Grant et al., 2001). Furthermore there are data to indicate that there are no appreciable differences evident when controlling for age of onset of first episode (Kumar, Bilker, Jin, Udupa, & Gottlieb, 1999).

Second, it appears that there are appreciable differences in neuropsychological functioning in terms of overall profile (i.e., patterns of strengths and weaknesses) for groups with Bipolar disorder and Psychotic spectrum diagnoses, and as a result their exclusion would be necessary (e.g., Basso & Bornstein, 1999; Schatzberg et al, 2000).

Third, inpatient versus outpatient status also has been shown to produce differing results and inclusion of one, but not both, of these groups would be ideal

(e.g., Basso, Lowery, Neel, Purdie, & Bornstein, 2002); Ilsley, Moffoot, & O'Carroll, 1995).

Fourth, whereas it was once assumed that antidepressants would impair neuropsychological functioning, evidence for this was limited to traditional tricyclic antidepressants and their effects on motor speed. Recent reviews and research investigations indicate that the newer antidepressants such as SSRIs do not have such effects (e.g., Kerr & Hindmarch, 1996; Moon & Vince, 1996) and to exclude persons on antidepressants would be of greater detriment as a sample selection bias.

Fifth, it has been shown that when examining populations who are depressed and have additional medical diagnoses, these diagnoses have no significant effect on neuropsychological performance if the groups are of similar educational levels and if persons with clear sensory or motor deficiencies arising from other neurological diagnoses are excluded from analyses (King et al., 1995).

Finally, the benefits of ideally administering a full neuropsychological battery are pivotal to providing adequate opportunity to attempt to interpret the integrity of complex brain systems. The battery would ideally be sensitive to cortical and subcortical dysfunction because both have been suspected as particularly relevant to depression.

Goals

There have been no previous research investigations conducted to differentiate participants with depression from those without depression, across different age groups, based on data from a comprehensive neuropsychological battery. Thus, the

current investigation is considered to be essentially exploratory. As a result, specific hypotheses are not generated. Alternately, the following goals are presented:

Goal 1: To apply cluster analytic algorithms to the neuropsychological data of participants diagnosed with and without depression, in separate procedures, for the child and adult groups. Cluster analytic methods will serve to differentiate subtypes of performance in most data sets and it is therefore expected they will also differentiate subtypes based on neuropsychological functioning across the battery used.

Goal 2: An examination of the internal validity of the groups will be conducted using multiple clustering algorithms so that the final cluster solutions selected are an accurate representation of the data, rather than the clustering technique utilized.

Goal 3: To examine if internally valid subtypes represent clusters that are comprised by a large majority of depressed participants. If groups or subgroups of depressed persons are differentiated, their pattern of neuropsychological functioning will be examined and interpreted in light of previous research findings particularly relevant to their developmental status (i.e., child and adult considerations).

Chapter II: Method

Participants

Participants in the study were 294 referred by neurologists, in the greater Indianapolis, Indiana area, to an independent clinic for neuropsychological evaluation. Participants considered for inclusion met the following criteria: (1) chronological age between 9 to 55 years inclusive; (2) overall Broad Cognitive Ability (BCA; Woodcock, McGrew, & Mather, 2001) within the non-impaired range (i.e., within 2.0 standard deviations of the mean); (4) data from every subtest of a complete neuropsychological assessment (i.e., participants were required to have data for 100% of tests in the assessment battery); (5) no primary sensory deficiency identified that would serve to prevent participation in the full test battery (5) Proficiency in English such that all subtests of the battery could be validly interpreted.

Participants were all suspected, or diagnosed, by their referring neurologists of having some neurological and/or psychiatric impairment. Incoming neurological diagnoses were rendered in accord with the International Classification of Diseases, Ninth Revision (ICD-9; American Medical Association, 2000). Incoming psychiatric disorder was diagnosed in accord with the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV; American Psychiatric Association, 1994). The sample was mixed for overall incoming diagnostic classification.

Participant age-based groups included 125 children between the ages of 9 and 15 years and 168 adults between the ages of 20 and 55 years. In the sample, 89%

reported right-hand dominance, 9% reported left-hand dominance, and 2% reported ambidexterity.

Measures

The Dean-Woodcock Neuropsychological Battery (Dean, 2003) was administered to each participant. This battery is comprised of a detailed Structured Interview, Mental Status Examination, the Woodcock-Johnson Tests of Cognitive Ability-Revised (WJ-R COG), the Dean-Woodcock Sensory-Motor Battery (DWSMB), and the Woodcock-Johnson Tests of Achievement. All portions of this battery were utilized in the current investigation with the exception of the Woodcock-Johnson Tests of Achievement.

Cognitive Abilities.

The Woodcock-Johnson Tests of Cognitive Ability-Revised (WJ-R COG) was utilized to provide data on cognitive abilities. The WJR-COG is based upon the Horn Cattell Gf-Gc theory of intellectual processing and measures seven broad intellectual abilities. A schematic diagram of these abilities and how they relate to other neuropsychological domains is presented in Figure 1. These abilities include fluid reasoning (Gf), comprehension-knowledge (Gc), visual processing (Gv), auditory processing (Ga), processing speed (Gs), short term memory (Gsm), and long-term retrieval (Glr). Administration of 14 subtests of cognitive ability provides seven cluster scores that represent each of these areas identified in Gf-Gc theory (Woodcock & Mather, 1990). Glr is comprised of the subtests Memory for Names and Visual-Auditory Learning. Gsm is comprised of the subtests Memory for Sentences

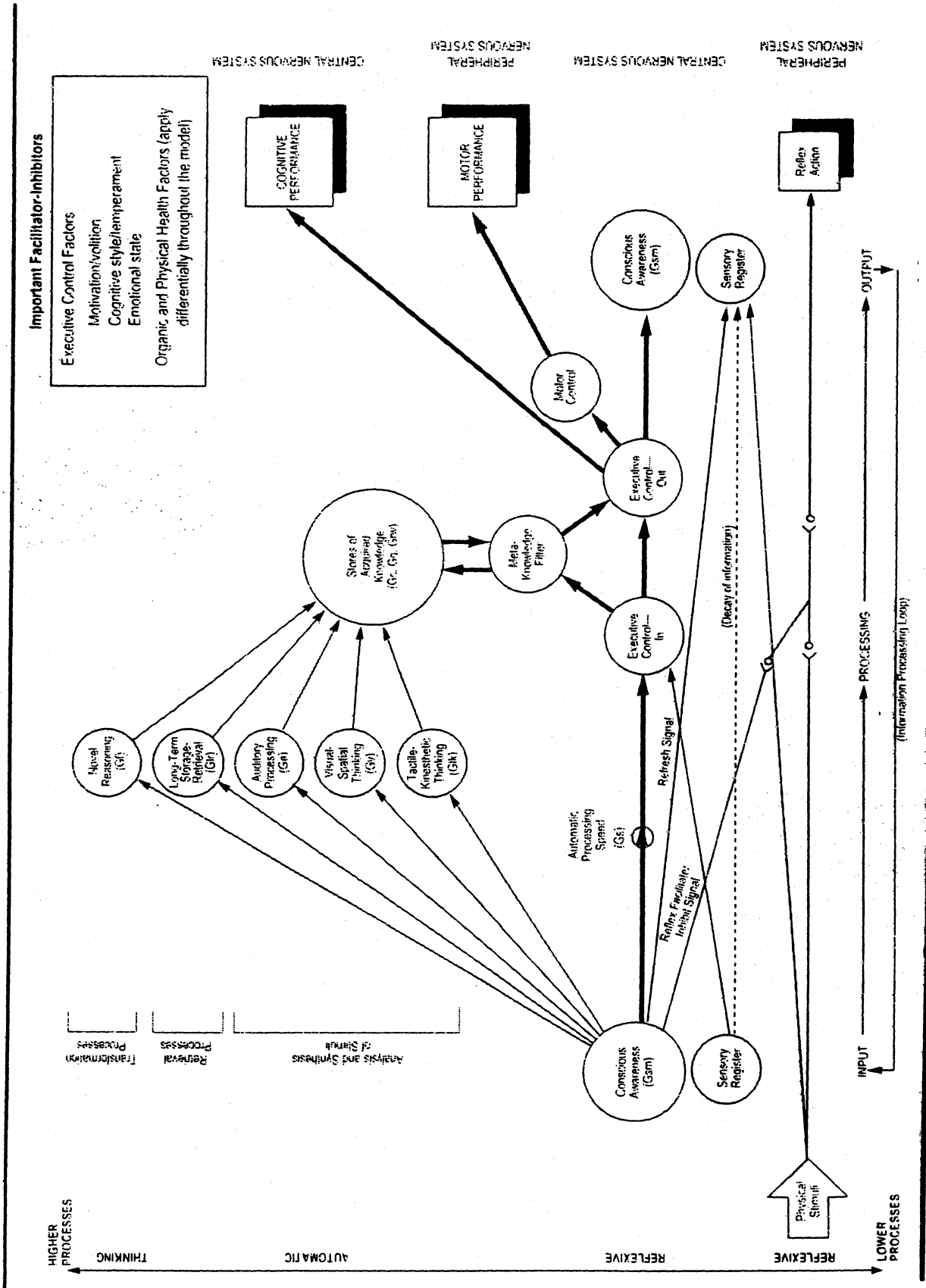

Figure 1. The Dean Woodcock Neuropsychology Model. Reprinted with Permission.

and Memory for Words, Gs is comprised of the subtests Visual Matching and Cross Out, Gz is comprised of the subtests Incomplete Words and Sound Blending, Gv is comprised of the subtests Visual Closure and Picture Recognition, Gc is comprised of the subtests Picture Vocabulary and Oral Vocabulary and Gf is comprised of the subtests Analysis-Synthesis and Concept Formation (Woodcock & Mather, 1990). Table 2 presents a description of each of the WJ-R COG subtests and their composite factors.

Woodcock & Mather's (1990) assessment of internal consistency of the WJ-R COG produced reliability coefficients ranging from .603 to .960 for individual tests, with a majority of coefficients falling in the .80s. Factor scores yielded reliability coefficients ranging from .734 to .989, with a majority of coefficients falling in the 90s (Woodcock & Mather, 1990). Woodcock & Mather's (1990) estimates of the validity correlations of the WJ-R COG were found to range between .523 to .729 when compared with more commonly used tests such as the Stanford-Binet-Fourth Edition and the Wechsler scales. Examination of construct validity yielded high intercorrelations within factors and low intercorrelations among the subtests (Woodcock & Mather, 1990).

Sensory and Motor Functioning.

Tests of sensory and motor functioning were those comprising the Dean-Woodcock Sensory Motor Battery (D-WSMB), which is part of the Dean-Woodcock Neuropsychological Battery (Dean & Woodcock, 2003). A schematic diagram of how the D-WSMB authors conceptualize motor functioning and how it relates

Table 2

Description of WJR-COG Subtests and Clusters

Subtests	Description and Constructs Measured
Glr	Long-term Storage-Retrieval (>30 seconds)
Memory for Names	Learning associations between unfamiliar auditory and visual stimuli
Visual-Auditory Learning	Associating unfamiliar rebuses with familiar words
Gsm	Short term Memory (<30 seconds)
Memory for Sentences	Repeating related words, phrases, and sentences
Memory for Words	Repeating unrelated words, phrases, and sentences

Gs	Processing Speed
Visual Matching	Rapidly locate and circle identical numbers in a row
Cross Out	Rapidly scan and compare similar drawings
Ga	Auditory Processing
Incomplete Words	Auditory closure of words missing phonemes
Sound Blending	Integration of phonemes to identify a whole word
Gv	Visual-Spatial Thinking
Visual Closure	Identification of altered and distorted pictures
Picture Recognition	Recognition of pictures after a 5-second delay
Gc	Comprehansion-knowledge/Crystallized Knowledge

	Picture Vocabulary	Recognize and name pictures objects
	Oral Vocabulary	Knowledge of word meanings
Gf		Novel Reasoning
	Analysis-Synthesis	Identifying missing components of a logic puzzle
	Concept Formation	Identifying underlying concepts in a stimulus set

to other neuropsychological domains is presented in Figure 1.

The D-WSMB is comprised of 18 subtests. Nine subtests are primarily devoted to sensory functioning and the other nine are devoted primarily to motor functioning. The combination of subtests chosen for this measure have a history of pathognomonic measurement and have been shown to have significant diagnostic utility in identifying cerebral dysfunction (Dean & Woodcock, 1999).

The nine subtests with a predominant sensory focus cover Lateral Preference, Visual Acuity, Visual Confrontation, Naming Pictures of Objects, Auditory Perception, Tactile, Perception with Palm Writing (letters and numbers), Tactile Perception with the Recognition of Objects, Finger Identification, and Simultaneous Localization of tactile perception (hands only and hand/cheek). The motor section is comprised of Mime Movements, Left-Right Movement, Finger Tapping, Expressive Speech, Strength of Grip, and two graphomotor construction tasks (drawing of a cross and a clock). In addition, three measures of subcortical functioning are included in this section. They are Gait and Station, Coordination with Finger-to-Nose and Hand/Thigh, and Romberg testing for unsteadiness (Dean & Woodcock, 1999).

Table 3 presents a description of the constructs measured by each subtest. The D-WSMB was considered an appropriate battery for the current study, most notably because of its three underlying factors related to simple sensorimotor, complex sensorimotor, and subcortical functioning. It was thought that this three-factor structure would allow for ease of discussion pertaining to multiple brain areas

Table 3
Description of D-WSMB Subtests

Subtests	Constructs Measured/Task
Lateral Preference	Handedness/laterality
Near Point Visual Acuity	Visual Acuity Screen
Visual Confrontation	Peripheral visual acuity/visual field cuts
Naming of Pictures of Objects	Dysnomia, aphasia, and color anomia
Auditory Perception	Auditory acuity screen
Palm Writing	Graphesthesia
Letters (simple)	Presentation of X's and O's to palms
Numbers (complex)	Presentation of numbers to palms
Object Identification	Presentation of common objects to palms; measure of astereognosia
Finger Identification	Measure of finger agnosia/asomatognosia

Simultaneous Localization	Measure of asomatognosia and tactile projection
Hands Only	Touch to back of hands
Hand/Cheek	Touch to hands and cheeks
Gait & Station	Peripheral and central nervous system functioning
Romberg Testing	Unsteadiness indicative of possibly subcortical dysfunction
Feet Together	Classic Romberg with arms crossed and eyes closed
Heel-to-toe	One foot in front of the other; lower extremity coordination
One Foot	Standing on one foot; lower extremity strength
Coordination	Ataxia, dyskinesia, and myoclonic jerks
Finger to nose	Fine motor coordination, dysmetria.
Hand/Thigh	Gross motor coordination, rapid alternating movements
Construction	Visuospatial ability; construction dyspraxia

Cross	Drawing a cross with a model
Clock	Drawing a round clock without a model
Mime Movement	Ideomotor movement
Left-Right Movement	Movement upon command; left-right confusion
Finger Tapping	Manual dexterity and speed
Expressive Speech	Central dysarthria
Strength of Grip	Strength of upper extremities

affected by suspect brain systems. Because the D-WSMB is a relatively new battery, a brief review of research on some of its properties is presented.

Two studies in support of the existence of the D-WSMB three factor model are noteworthy. Lewis (1998) conducted an exploratory factor analysis for data on the D-WSMB with 441 participants. There were three underlying factors identified: (1) a complex sensory motor factor, (2) a simple sensory factor, and (3) a subcortical motor factor. In another study, Hill, Lewis, Dean, & Richard (2000) conducted a principal components analysis on data from 617 participants 2-88 years of age. Results supported a similar 3-factor solution accounting for 50.9 % of the variance, concluding that their findings provide support for the underlying constructs of the D-WSMB.

One frequently criticized feature of sensory and motor tests is on the interrater reliability. The interrater agreement of the D-WSMB has been examined in this regard. Woodward, Ridenour, Dean, and Woodcock (2002) examined characteristics of the D-WSMB for item discrimination, objectivity of time categories, item independence, item number, scale of measurement, item heterogeneity, and estimated the agreement of independent ratings on portions of the battery that require examiners to make judgments about level of functioning. Using criteria for evaluation proposed by Ciccheti et al. (1992), Woodard et al. (2002) estimated and qualified the interrater agreement and the reliability of the sensorimotor battery using the significance of Kappa. They obtained inter-rater reliability coefficients ranging from .690 to 1.00 with the majority falling in within the .900's. Thus, using the Ciccheti et al. (1992)

criteria for evaluation, the vast majority of results were *Good* to *Excellent*, where *Good* stands for .60-.74 and *Excellent* stands for >.75 for the weighted kappa values. Results also indicated that item homogeneity was high, which the authors purported would reduce the risk of false positive decisions.

Procedure

The Dean-Woodcock Neuropsychological Battery (Dean, 2003) was administered to each participant. As previously mentioned, this battery is comprised of a detailed Structured Interview, Mental Status Examination, the Woodcock-Johnson Revised Cognitive Battery, the Dean-Woodcock Sensory-Motor Battery, and the Woodcock-Johnson Tests of Achievement.

All portions of this battery were utilized in the current investigation with the exception of the Woodcock-Johnson Tests of Achievement. All participants were administered a clinical interview and mental status examination by the same experienced, licensed clinical neuropsychologist and returned a second day for standardized testing. Standardized testing was followed by completion of either the Personality Inventory for Children-Revised (PIC-R; Wirt, Lachar, Klinedinst, & Seat, 1982) or the Minnesota Multiphasic Personality Inventory (MMPI; Hathaway & McKinley, 1983), based upon the age of the participant.

All tests were administered by well-trained psychometrists in a quiet room designated for neuropsychological testing with only the participant and psychometrist present in the room.

For participants under 18 years of age, the nature of the assessment was discussed with the legal guardian(s) or parent(s) present and consent to continue with the evaluation was obtained. For participants 18 years of age and older, upon entry into the testing room, each participant was greeted by the examiner and explained the nature of the assessment. Following consent to continue each participant was administered the D-WSMB and the WJ-R COG along with selected portions of the Woodcock-Johnson Revised Tests of Achievement (WJ-R ACH). As previously mentioned, the participants' achievement scores were not used in the current study. Total examination time ranged between 90 and 180 minutes.

Following completion of all testing, the nature of the testing was once again reviewed as was the procedure for obtaining results. For participants under 18 years of age, legal guardian(s) or parent(s) that were present were also debriefed in this manner.

All participants met with the same licensed clinical neuropsychologist to review the test results in a follow-up visit. Depression diagnoses were determined by the same experienced, licensed clinical neuropsychologist based upon information provided in the structured clinical interview portion of the D-WNAB and in accord with classification criteria for Major Depressive Disorder outlined in the DSM-IV. Patients identified as meeting DSM-IV criteria for Bipolar Disorder or Psychosis were excluded from the present investigation. Information from the personality inventories was not used to include participants in either depression or non-depression diagnostic groups. However, results from these inventories were used to

exclude participants from group inclusion if data obtained were contradictory to the status of a depression diagnosis (e.g., if patterns of response bias were evident).

Participants who did not complete 100% of tests in the full battery were excluded. Percent diagnoses in the clinical sample is presented in Table 3.

Table 3
Percent Diagnoses In the Mixed Clinical Sample

	Child		Adults	
SAMPLE	Nondep.	Dep.	Nondep.	Dep.
ADHD NOS	11	12	3	4.5
ADHD - inattentive	4	4	1.2	1.3
ADHD - combined	0	0	0	0
ADHD - hyperactive-impulsive	0	0	0	0
Affective Spectrum Disorder	0	0	0	0.7
Depression	0	100	0	100
Reactive Attachment d/o	2	0	0	0
Leukemia	1	0	0	0
Anxiety	7	7	15.5	15
Brain Tumor	1	0	0	0.7
CV Disease	0	0	0	1.3
CV Disease - Angioma	1	0	0	0
CVA	0	0	3.7	4
CV Disorder	0	0	1.2	0.7
Conduct d/o	2	4.2	1.2	0
Polysubstance Abuse	0	0	0	0.7
Hydrocephalus	1	0	1.2	0
Hypoxia	0	0	1.2	0
Infectious disease	0	0	1.2	0
Communication d/o	4	0	0	0
Mixed Expressive/Receptive Lang	2	0	0	0
LD NOS	1	0	2.4	0.7
Reading Disorder	4.5	0	1.2	0
Multiple Sclerosis	0	0	2.4	0.7
Cerebral Palsy	1	0	1.2	0.7
Genetic d/o; congenital d/o	0	0	0	0
Prenatal teratogen exposure	1	0	0	0
Adjustment Disorder	0	2.1	0	0
PDD - NOS	4	2	4.8	0
Autism	1	0	0	0
Aspergers	0	0	0	0.7
Seizure	6	0	3.6	2
Seizures - complex partial	0	0	0	0
Seizures - general absence	0	2.1	0	0
TBI NOS	4	0	4.8	1.3
CHI NOS	1	4.2	7.1	4.7
CHI mild	1	0	4.8	2.7
CHI severe	1	0	0	0
Concussion	1	0	3	4
Tourettes	2	2.1	0	0
Anorexia	0	0	0	0.7
General Medical Condition	1	0	0	2
Borderline Personality Disorder	0	0	0	0.7

Chapter III: Results

Overview of Data Analyses

The current investigation was conducted to see if it would be possible to differentiate groups of participants with and without depression based on data from a comprehensive neuropsychological assessment. To this end, the data were analyzed to satisfy three main goals.

Goal 1: To apply cluster analytic algorithms to the neuropsychological data of depressed and non-depressed participants. The child and adult groups will be analyzed separately in this regard. Because cluster analytic methods will serve to differentiate groups in most data sets, it was expected they would also differentiate groups based on neuropsychological functioning across the battery in the current investigation.

Goal 2: To examine the internal validity of the groups using multiple clustering algorithms so that the final cluster solutions selected were an accurate representation of the data, rather than the clustering technique utilized.

Goal 3: To examine if internally valid solutions represent groups or subgroups that are comprised by a large majority of depressed participants. If groups or subgroups of depressed persons are differentiated, their pattern of neuropsychological functioning will be examined and interpreted in light of previous research findings particularly relevant to their developmental status (i.e., child and adult considerations).

Data Analyses

Data were analyzed by grouping participant results into two age-based groups (i.e., child and adult) that were decided upon with the minimization of variability in mind, as determined by previous research studies using the current battery. Data were not divided to examine sex differences as there has been no precedent set in the depression literature to do so and because it has been shown that sex differences on the D-WNAB and the interaction between sex and age are not significant (Arceneaux, Hill, Chamberlain, & Dean, 1997).

To achieve *Goal 1* and *Goal 2,* cluster analysis was conducted as the main method of data analysis. Cluster analysis identifies an optimal solution of groupings that minimizes within group variance and is particularly suited for the current investigation (Adams, 1985; Hair & Black, 2000). Cluster Analysis was also selected based on its utilization in previous, similar research investigations (e.g., Donders, 1996; Murji et al., 2003; Saunders, 2000; Wiegner, & Donders, 1999). SPSS version 11 was used for all data analyses.

Because the current investigation was designed to determine if data from a comprehensive neuropsychological examination would reliably identify groups of participants with depression, variables across the full neuropsychological battery were selected for inclusion in the analyses. The ability summary scores derived from the neuropsychological battery were selected from the cognitive portion for inclusion in the analyses. These were fluid reasoning (Gf), comprehension-knowledge (Gc), visual processing (Gv), auditory processing (Ga), processing speed (Gs), short term

memory (Gsm), and long-term retrieval (Glr). There are no ability summary scores produced for the sensory perceptual, motor, and subcortical data in the sensorimotor battery used in the current investigation. Based on information obtained from a review of literature on the sensorimotor battery (e.g., Hill, Dean, & Woodcock, 2000), data from one subtest that was considered most representative of each main sensorimotor section was selected as a variable in the analyses. For the sensory perceptual data, simple tactile perception was selected. The test of grip strength was selected from the motor subtest. Gait and station functioning were selected from the subcortical section. Right/Left scores for the sensory perceptual and motor data were included as distinct variables to facilitate qualitative interpretation of right/left differences. Data were standardized based on age utilizing the clinical sample as the population. Descriptive statistics were compiled and are presented in Table 4.

A two-stage clustering procedure was conducted utilizing three different clustering methods. Three different clustering methods were utilized because cluster analytic methodology produces groups of subjects, even in random data, that may, in essence, be representative of the particular clustering method rather than the data (Fuerst et al., 1989). Selection of the three clustering methods was based on exploration of all available methods through SPSS, quantitative analyses of the cluster solutions for these methods, and qualitative interpretation of the cluster solutions. Specifically, all clustering methods available through SPSS version 11 were initially utilized to explore the cluster solutions. The methods that produced the best cluster solutions were utilized for internal validity (i.e., reliability) purposes.

Table 5

Descriptive Statistics

Child Group N=121

	Age (years) Mean (SD)	Education Mean (SD)	Males	Females
Depressed	12.19 (1.97)	6.29 (2.23)	26	18
Non-Depressed	12.17 (1.74)	6.37 (2.04)	59	18

Adult Group N=168

	Age Mean (SD)	Education Mean (SD)	Males	Females
Depressed	39.66 (9.51)	12.79 (2.56)	47	69
Non-Depressed	40.63 (10.50)	13.18 (2.71)	22	30

Selection of cluster solutions was conducted by examination of the dendograms, agglomeration schedules, and cluster centers. Ward's (1963) minimum variance method, Between Groups (Average) linkage, and Centroid Methods were selected as the agglomerative hierarchical clustering methods for the adult groups. For the child groups, Ward's minimum variance method, Complete Linkage, and Centroid methods were selected. Squared Euclidian distance was used as the measure of similarity between case pairs.

The selected clustering analytic algorithms were re-run utilizing K-means iterative partitioning. The cluster means were plotted with cluster variables on the x-axis and standardized scores on the y-axis. Visual inspections of graphs were conducted to explore the interpretability of the neuropsychological characteristics of each cluster. To examine the replicability of clusters across the various cluster analytic algorithms for the methods, nominal measure of association analyses were conducted. The cluster solutions were examined to determine if a diagnosis of depression could characterize the subgroups (i.e., external validation for a depression-based solution). The above-mentioned procedures were conducted for the child and adult groups separately.

Cluster Analytic Findings

Examination of the resulting agglomerative schedules and dendogram configurations from the hierarchical agglomerative clustering techniques (specified for a solution of 2 to 15 clusters) indicated that a 4-cluster solution would likely best represent the adult data from the present study for the selected methods. At the

exploratory stage, both a 3-cluster solution and a 4-cluster solution appeared possible for the child data for the selected methods. A 4-cluster child solution was rejected because it appeared that one of the clusters was consistently comprised of a combination of a small number of participants (n=4). The cluster membership in this small cluster was not consistent across methods.

Case-by-case examination indicated that across the methods, different combinations of these four cases would either cluster together in the abovementioned small cluster with or would, individually, be resistant to clustering with any other case and remain as singleton. By discarding these four cases, there was a clear three-cluster solution across the three main methods utilized.

Final cluster centers from the hierarchical agglomerative analyses were then used as the seed values for the K-means iterative partitioning method relocation pass for both child and adult data. This was done to correct for possible fusion errors during the initial stage of clustering across the three two-stage cluster analyses with all methods utilized for each of the child and adult groups. The resulting pseudo F-statistics and interpretability and clinical relevance for each cluster solutions were examined for the final number of clusters across the methods used. The latter qualitative analyses have proven effective for determining the best number of clusters across all techniques and samples (Everitt, 1980). Specific attention was directed to the replicability and clinical interpretability (qualitative analyses) during evaluation of the adequacy of the clusters solutions because these qualitative methods had been successfully utilized in previous investigations (e.g., Fuerst, 1991).

Based upon all of the above evaluations, a four-cluster solution was maintained as providing the best solution (i.e., it appeared to provide the best quantitative and qualitative solution) for each of the clustering algorithms used in the adult data and a three-cluster solution was maintained as providing the best solution for each of the clustering algorithms in the child data. For both the child and adult cluster solutions, the differences between individual clusters appeared to be represented by ability level on all variables aside from simple tactile perception. To facilitate ease of discussion of the results, the clusters were given names that appeared to capture their unique qualities. Adult clusters across all three methods appeared to yield an Above Average level cluster, Average level cluster, Low Average level cluster, and Below Average level cluster. Means and standard deviations for each of the clusters across the methods that were utilized in the transformations are presented in Tables 5-7 for the adult participant group and Table 8 for the child participant group and are presented in T-scores metric to facilitate interpretation when visually inspecting the graphs. Figures 2 to 4 represent the cluster solutions across the adult methods used.

Ward's method and Between Groups (Average) methods appeared to be the most similar based upon visual inspection, with the Centroid cluster solution also appearing quite similar to these methods. The three-cluster child solutions grouped all participants within the same clusters (i.e., exact replication), therefore one graph, Figure 5, represents this cluster solution. For the child clusters, across all three

Table 5
Adult Mean T-Scores and Standard Deviations (SD) for Wards' Method

		Gait & Station	Grip Strength-R	Grip Strength-L	Simple Tactile-R	Simple Tactile-L	GLR	GSM	GS	GA	GV	GC	GF
1	Mean	53.01	56.87	56.38	49.62	51.07	59.62	58.70	57.71	57.47	57.55	58.29	61.67
	SD	5.64	8.42	8.31	12.58	0.16	6.72	7.03	6.90	7.73	7.22	7.16	6.23
2	Mean	52.25	45.20	44.50	51.88	51.06	51.57	50.26	52.00	51.79	51.25	51.29	49.99
	SD	6.36	5.12	5.31	0.56	0.32	7.60	8.12	8.01	7.70	7.60	7.62	6.22
3	Mean	48.62	60.01	61.32	50.75	51.06	42.74	47.52	45.93	44.41	46.12	48.28	45.17
	SD	12.36	7.85	6.45	2.02	0.48	8.12	9.74	7.47	8.53	9.61	7.32	6.76
4	Mean	43.18	40.10	41.03	45.10	44.66	40.96	39.80	38.72	41.47	40.64	37.15	39.07
	SD	15.27	5.82	5.35	18.99	24.60	6.84	7.15	9.14	10.13	10.09	8.52	8.38

Note. 1=Above Average, 2=Average, 3=Low Average, and 4= Below Average

Table 6
Adult Mean T-Scores and Standard Deviations (SD) for Between Groups (Average) Method

		Gait & Station	Grip Strength-R	Grip Strength-L	Simple Tactile-R	Simple Tactile-L	GLR	GSM	GS	GA	GV	GC	GF
1	Mean	53.01	56.87	56.38	49.62	51.07	59.62	58.70	57.71	57.47	57.55	58.29	61.67
	SD	5.64	8.42	8.31	12.58	0.16	6.72	7.03	6.90	7.73	7.22	7.16	6.23
2	Mean	52.25	45.22	44.79	51.88	51.06	51.47	50.46	51.95	51.80	51.15	51.30	49.98
	SD	8.91	5.08	5.82	0.56	0.32	7.59	8.23	7.96	7.64	7.59	7.56	6.17
3	Mean	50.44	60.43	61.20	50.75	51.06	42.68	47.00	45.86	44.15	46.17	48.16	45.04
	SD	8.91	7.58	6.51	2.02	0.48	8.23	9.41	7.58	8.54	9.77	7.40	6.83
4	Mean	43.18	40.09	41.03	45.09	44.66	40.96	39.80	38.72	41.47	40.64	37.15	39.07
	SD	15.27	5.82	5.35	18.99	24.60	6.84	7.15	9.14	10.13	10.09	8.52	8.38

Note. 1=Above Average, 2=Average, 3=Low Average, and 4= Below Average

Table 7
Adult Mean T-Scores and Standard Deviations (SD) for Centroid Method

		Gait & Station	Grip Strength-R	Grip Strength-L	Simple Tactile-R	Simple Tactile-L	GLR	GSM	GS	GA	GV	GC	GF
1	Mean	52.25	58.08	57.47	49.62	51.06	59.59	58.06	58.28	58.03	58.33	59.16	61.93
	SD	5.82	7.86	7.99	13.26	0.16	6.65	7.07	6.30	7.84	6.61	6.31	6.48
2	Mean	52.25	45.45	45.09	51.88	51.06	52.62	51.87	51.80	51.71	51.31	52.06	51.14
	SD	8.73	5.22	5.86	0.56	0.32	7.40	8.50	8.28	7.42	7.72	6.98	6.13
3	Mean	50.44	60.32	61.05	50.75	51.06	42.56	46.44	46.15	44.48	46.06	47.95	44.77
	SD	8.91	7.71	6.72	2.02	0.48	8.25	9.23	7.70	8.74	9.66	7.36	6.80
4	Mean	44.99	40.66	41.38	46.23	46.26	41.32	40.72	40.91	43.05	42.01	37.59	39.73
	SD	14.55	5.65	5.38	17.53	22.54	6.91	7.56	10.01	10.63	10.13	8.14	7.93

Note. 1=Above Average, 2=Average, 3=Low Average, and 4= Below Average

Table 8
Child Mean T-Scores and Standard Deviations (SD) for Ward's, Complete Linkage, and Child Methods

		Gait & Station	Grip Strength-R	Grip Strength-L	Simple Tactile-R	Simple Tactile-L	GLR	GSM	GS	GA	GV	GC	GF
1	Mean	52.19	54.06	53.34	50.00	51.33	55.86	57.92	56.88	55.73	55.08	58.51	57.81
	SD	0.32	10.07	10.00	0.00	1.69	8.54	3.69	7.61	9.09	8.08	6.87	5.65
2	Mean	49.99	49.82	49.97	50.00	50.00	48.99	49.40	49.09	49.40	49.67	48.93	49.07
	SD	10.68	9.37	8.95	0.49	2.37	8.81	6.05	7.60	7.94	9.82	5.36	6.99
3	Mean	45.73	42.15	41.73	50.00	46.40	42.84	35.73	37.95	39.49	41.97	36.51	37.54
	SD	17.47	5.31	7.21	0.00	77.97	8.56	7.41	6.80	6.84	8.08	5.71	9.10

Note. 1=Above Average, 2=Average, 3=Low Average

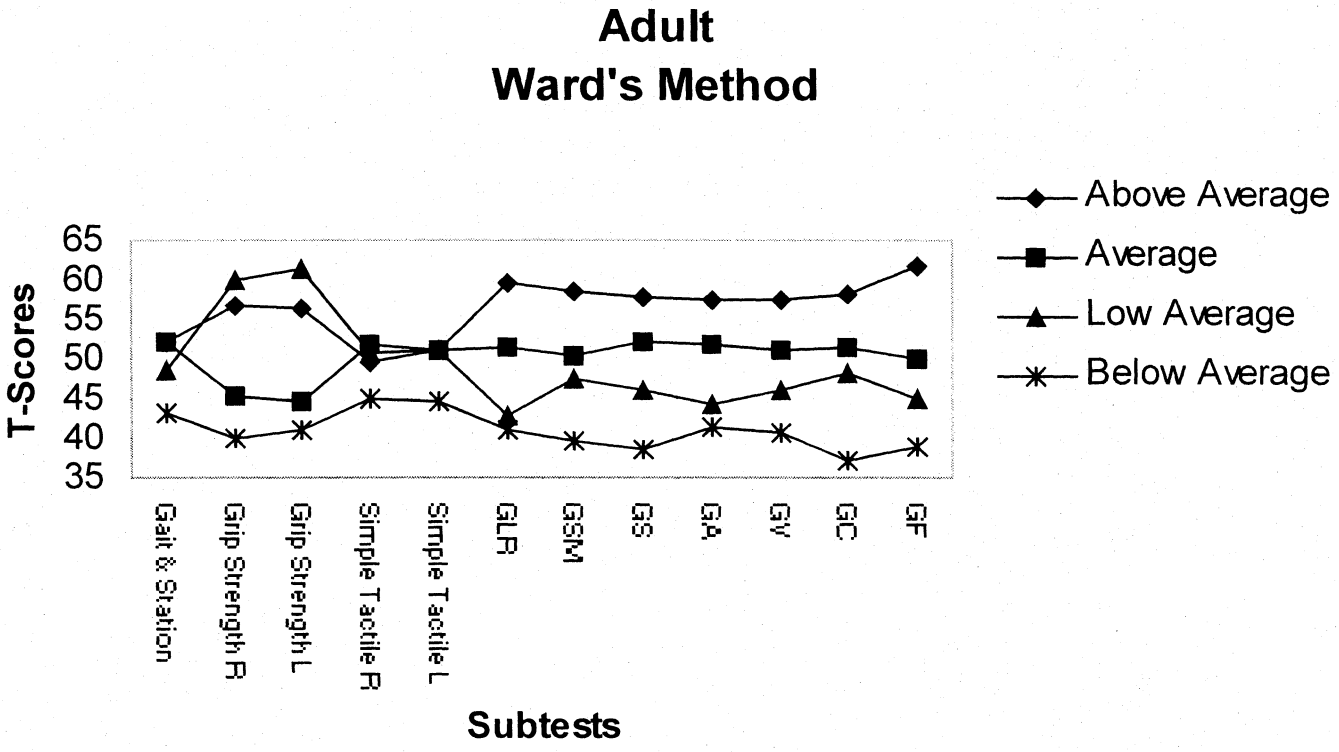

Figure 2. Adult mean cluster values using Ward's method.

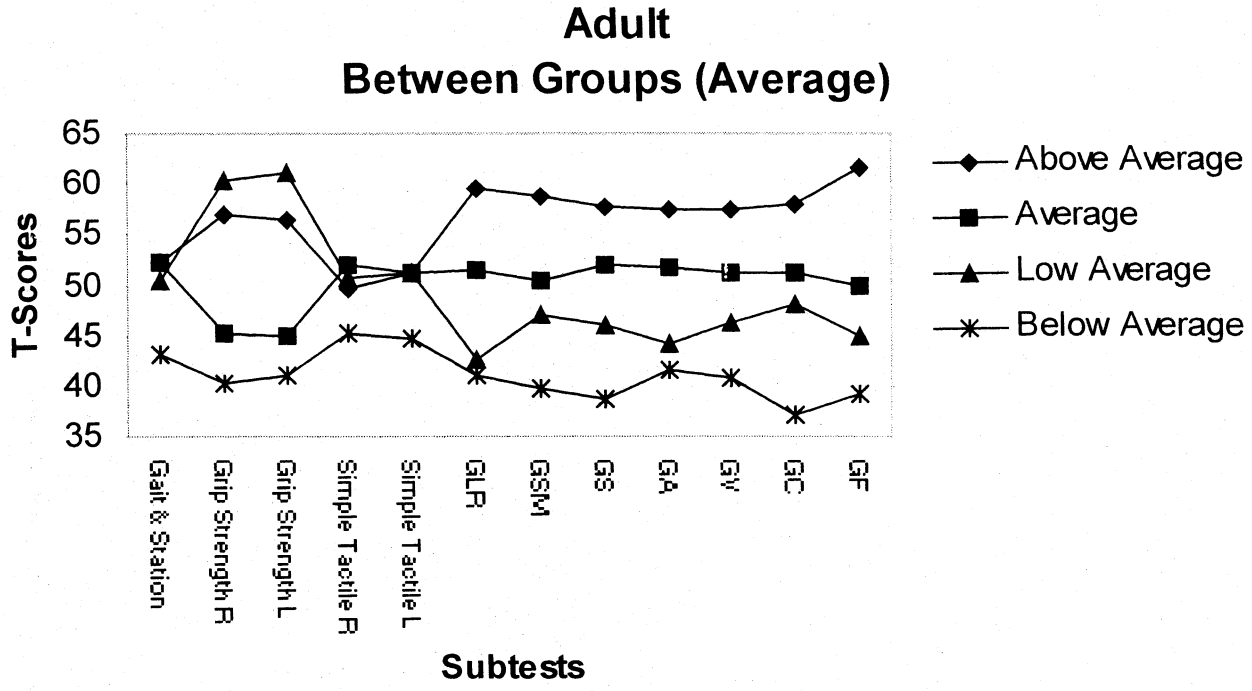

Figure 3 . Adult mean cluster values using Between Groups (Average) method.

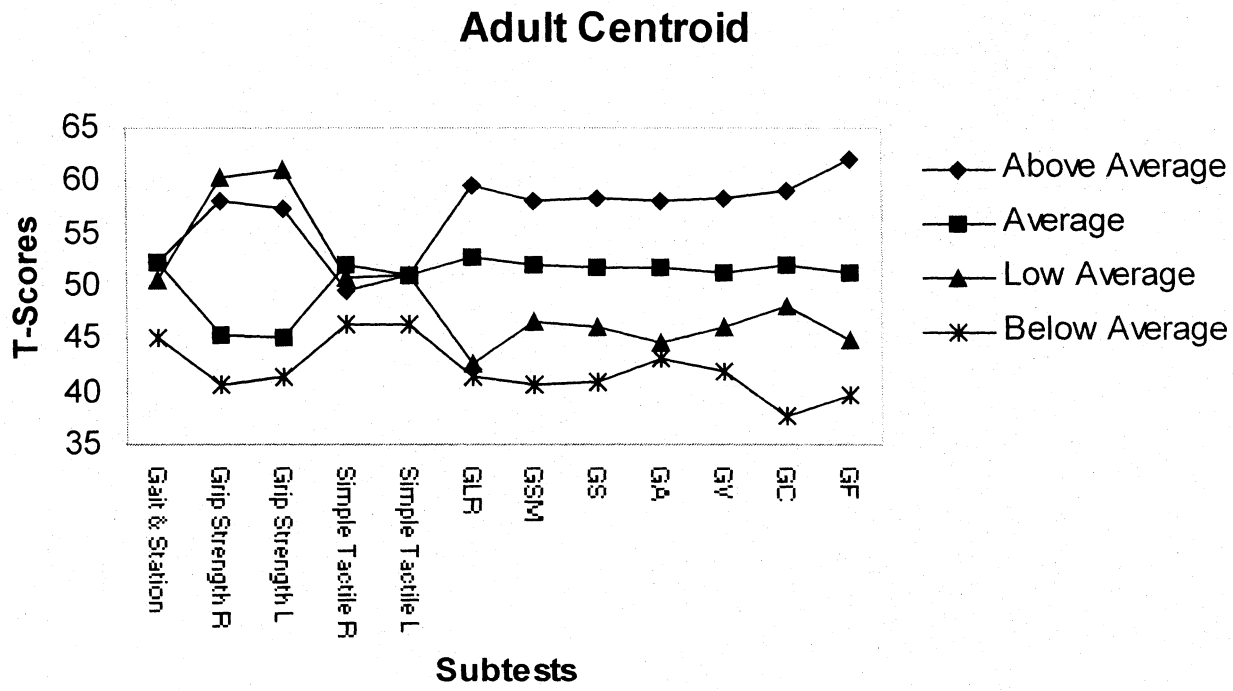

Figure 4 . Adult Mean Cluster Values using Centroid method.

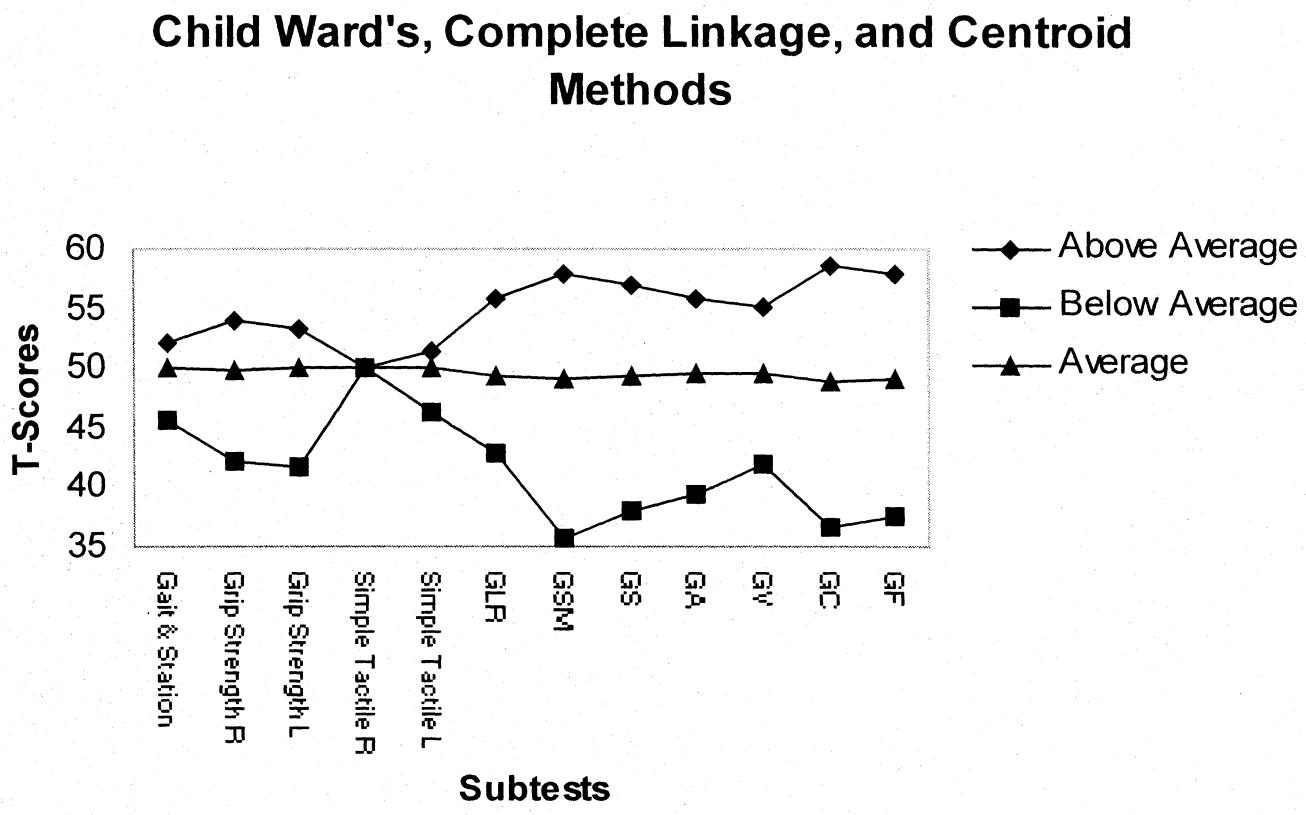

Figure 5. Child Mean Cluster Values for Ward, Complete Linkage, and Centroid Methods

methods, there appeared to be an Above Average level cluster, an Average level cluster, and a Below Average level cluster.

To examine the replicability of clusters across the various cluster analytic algorithms for the adult methods, nominal measure of association analyses were conducted. Coefficients of association between the three cluster algorithms employed for the adult data are presented in Table 9. All Lambda and Goodman and Kruskal's tau coefficients for the various child solutions had a value of 1.00 for the methods of association analyses and were found to be significant at the $p<.001$ level. Thus, a significant level of association between the cluster solutions generated using the various techniques was obtained for both the child and adult groups. This finding suggests that the four clusters were replicated with good accuracy by Ward's, Between Groups (Average), and Centroid methods for the adult data and by Ward's, Complete Linkage, and Centroid methods for the child groups.

To achieve *Goal 3* the percentage of participants with a diagnosis of depression was examined. Inspection of Table 10 clearly indicated that there were no appreciable differences for depression diagnosis between the clusters. The percentage of participants across the clusters provided a close representation of the percentage of participants in the adult sample. The percentage of children with a diagnosis of depression was examined and is summarized in Table 11. Inspection of the percentage of participants with a diagnosis of depression in the child groups did not indicate any major differences, however an analysis of variance was conducted to confirm this finding. Results indicated that there were no significant differences (i.e.,

Table 10

Adult Lambda and Goodman and Kruskal's Tau Measurements of Association Between the Three Cluster Analysis Algorigthms Utilized

Method	Ward's		Between Groups (Average)		Centroid	
	Lambda	Tau	Lambda	Tau	Lambda	Tau
Ward's	-		.990	.984	.879	.820
Between Groups (Avg.)	.990	.984	-		.889	.834
Centroid	.879	.817	.888	.832	-	

Note. Lambda and Tau values are presented with the methods in the columns as the dependent variable. All values contained in the table were significant at greater than the $p < 0.001$ level.

Table 11
Percent of Depressed and Non Depressed Participants in Each Cluster Across Methods Used for the Adult Data

		%Depressed	%Non-Depressed
Ward's			
n=39	Above Average	67	33
n=69	Average	68	32
n=33	Low Average	70	30
n=27	Below Average	67	33
Between Groups (Average)			
n=39	Above Average	68	32
n=70	Average	70	30
n=32	Low Average	68	32
n=27	Below Average	67	33
Centroid			
n=35	Above Average	69	31
n=69	Average	71	29
n=32	Low Average	69	31
n=32	Below Average	68	32

Table 12
Percent of Depressed and Non Depressed Participants in Each Cluster Across Methods Used for the Child Data

		%Depressed	%Non-Depressed
Ward's Method Complete Linkage Centroid			
n=50	Above Average	40	60
n=52	Average	38	62
n=19	Low Average	16	84

there were no differences that reached a significance level of $p<.05$) between percentage of participants with a diagnosis of depression utilizing analysis of variance.

Additional Data Analyses

There were no statistically significant differences across the cluster solutions for the child and adult data between the participants diagnosed with and without depression when utilizing the comprehensive neuropsychological test results. The decision to utilize measures across the full neuropsychological battery was based upon allowing for interpretation of the integrity of complex brain systems in the event that clusters were found comprised by significant proportions of participants with depression. Because this did not occur, consideration was given to further analyses of any specific areas of neuropsychological functioning that have been particularly suspect as deficient in persons with depression.

Sensorimotor and psychomotor functioning, such as reaction to stimuli and motor speed, have been long suspected as areas of deficiency in persons with depression (e.g., Rogers et al. 2000, Sobin and Sackeim, 1997). Thus, with a goal of exploring if sensorimotor data could serve to identify unique groups of depressed participants, the cluster analytic procedures utilized and outlined in the first set of analyses were repeated with sensorimotor data. The same procedures as outlined for the previous cluster analyses were followed for the child and adult groups utilizing sensorimotor data. Because there were no ability summary scores produced for the main sensory perceptual, motor, and subcortical statistically-derived main factors in

the sensorimotor battery, data from the subtests that were considered most representative of each main sensorimotor section were selected as a variables in the analyses. For the sensory perceptual data, simple tactile perception was selected. The test of grip strength was selected from the motor subtest. Gait and station functioning was selected from the subcortical section. Finger tapping was also included to provide a measure of psychomotor speed. Right/Left scores for the sensory perceptual and motor data were summed for the current analyses.

Additional Cluster Analytic Findings

Examination of the resulting agglomerative schedules and dendogram configurations from the hierarchical agglomerative clustering techniques (specified for a solution of 2 to 15 clusters) indicated that a 4-cluster solution would likely best represent the adult and child data from the present study for the selected methods.

Final cluster centers from the hierarchical agglomerative analyses were then used as the seed values for the K-means iterative partitioning method relocation pass for both child and adult data. This was done to correct for possible fusion errors during the initial stage of clustering across the two-stage cluster analyses with all methods utilized for each of the child and adult groups. The resulting pseudo F-statistics and interpretability and clinical relevance for each cluster solution were examined for the final number of clusters across the methods used. Based upon all of the above evaluations, a four-cluster solution was maintained as providing the best solution (i.e., it appeared to provide the best quantitative and qualitative solution) for each of the clustering algorithms used in the child and adult data. For the adult data,

Ward's, Within Groups (Average), and Complete linkage methods were deemed as providing the best replication of the 4-cluster solution. For the child data, Centroid, Between Groups (Average), and Complete Linkage were selected as providing the best solutions.

Means and standard deviations for each of the clusters across the methods that were utilized in the transformations are presented in Tables 12-14 for the adult participant group and Table 15 for the child participant group. Data are presented in T-Scores for ease of comparison across metrics and plotted in Figures 6-8 for the adult group. For the adult cluster solutions (see Figures 6-8), Cluster 1 was characterized by high-average finger tapping speed, low-average grip strength, and average simple tactile and gait and station performance. Cluster 2 was comprised by high-average finger tapping speed, above average grip strength, and average simple tactile and gait and station performance. Cluster 3 was comprised of average performance across all tests. Cluster 4 was comprised of below average finger tapping speed and grip strength, with average simple tactile and gait and station performance. Thus, performance was generally average for simple tactile and gait and station tests, however differing levels of performance in finger tapping speed and grip strength provided unique characteristics to the clusters in the solution.

The four-cluster child solutions grouped all participants within the same clusters (i.e., exact replication), therefore one graph, Figure 9, represents this cluster solution. Inspection of the child cluster graphs indicated minimal differences on

Table 13

Adult Mean T-Scores and Standard Deviations (SD) for Ward's Method Using Sensory Motor Data

		Tapping	Grip	Simple Tac	Gait & Station
1	Mean	56.23	44.50	50.20	50.30
	SD	5.14	3.25	9.54	11.27
2	Mean	55.55	64.60	51.70	54.40
	SD	9.30	5.00	0.83	8.00
3	Mean	50.75	52.47	51.70	50.44
	SD	14.81	12.39	1.86	0.57
4	Mean	38.60	40.00	45.70	48.60
	SD	8.53	4.71	17.22	10.36

Table 14

Adult Mean T-Scores and Standard Deviations (SD) for Within Groups (Average) Method Using Sensory Motor Data

		Tapping	Grip	Simple Tac	Gait & Station
1	Mean	55.21	45.64	50.28	50.65
	SD	5.41	2.46	9.26	10.91
2	Mean	50.35	54.44	51.00	50.60
	SD	5.81	2.80	0.56	10.00
3	Mean	39.85	39.85	46.67	48.06
	SD	8.78	4.75	16.11	10.18
4	Mean	55.69	66.31	51.79	51.03
	SD	10.30	4.46	0.83	8.36

Table 15

Adult Mean T-Scores and Standard Deviations (SD) for Complete Linkage Method Using Sensory Motor Data

		Tapping	Grip	Simple Tac	Gait & Station
1	Mean	55.21	45.64	50.28	50.65
	SD	5.37	3.28	8.98	10.54
2	Mean	55.69	66.31	51.79	51.03
	SD	9.97	4.60	0.83	8.18
3	Mean	50.36	54.44	51.00	50.99
	SD	8.36	4.85	16.85	10.36
4	Mean	39.85	39.85	46.67	48.06
	SD	5.79	2.65	1.48	10.18

Table 16

Child Mean T-Scores and Standard Deviations (SD) for All Methods Utilized for Sensory Motor Data

Title child SM

	Tapping	Grip	Simple Tac	Gait & Station
1 Mean	56.44	51.04	51.24	50.64
SD	5.49	4.17	6.93	6.47
2 Mean	48.44	40.94	49.78	51.07
SD	6.41	6.08	0.99	0.02
3 Mean	56.25	66.75	51.15	52.20
SD	8.31	3.73	0.99	17.47
4 Mean	34.81	45.50	47.07	45.47
SD	5.89	3.88	21.78	7.12

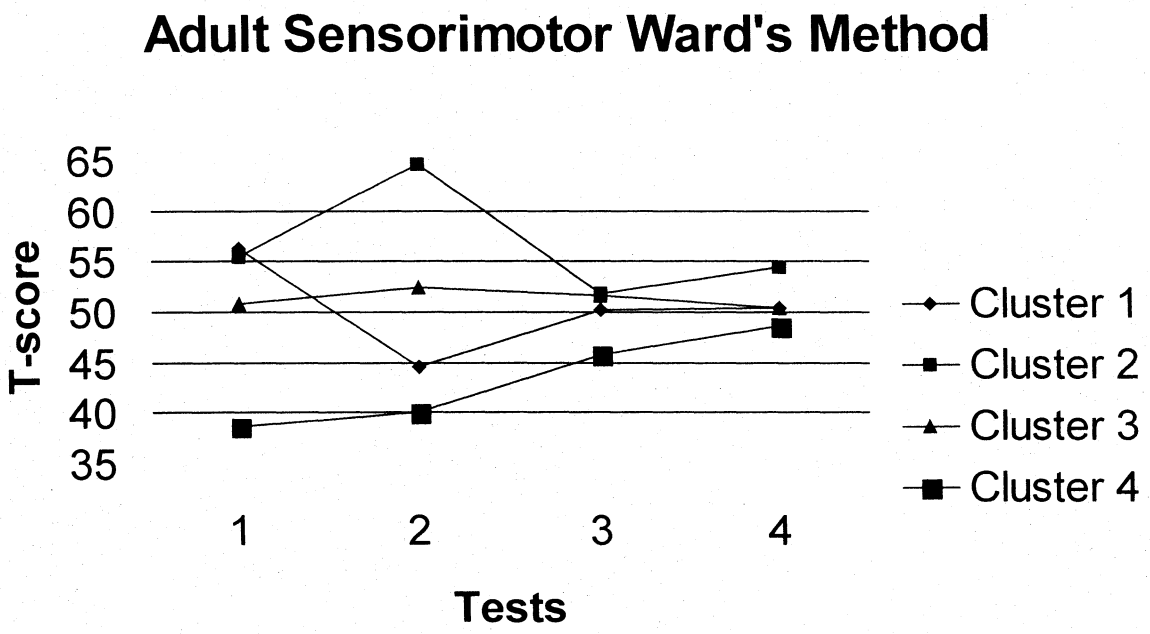

Figure 6. Adult Mean Cluster Values for Ward's Method, Additional Analyses.

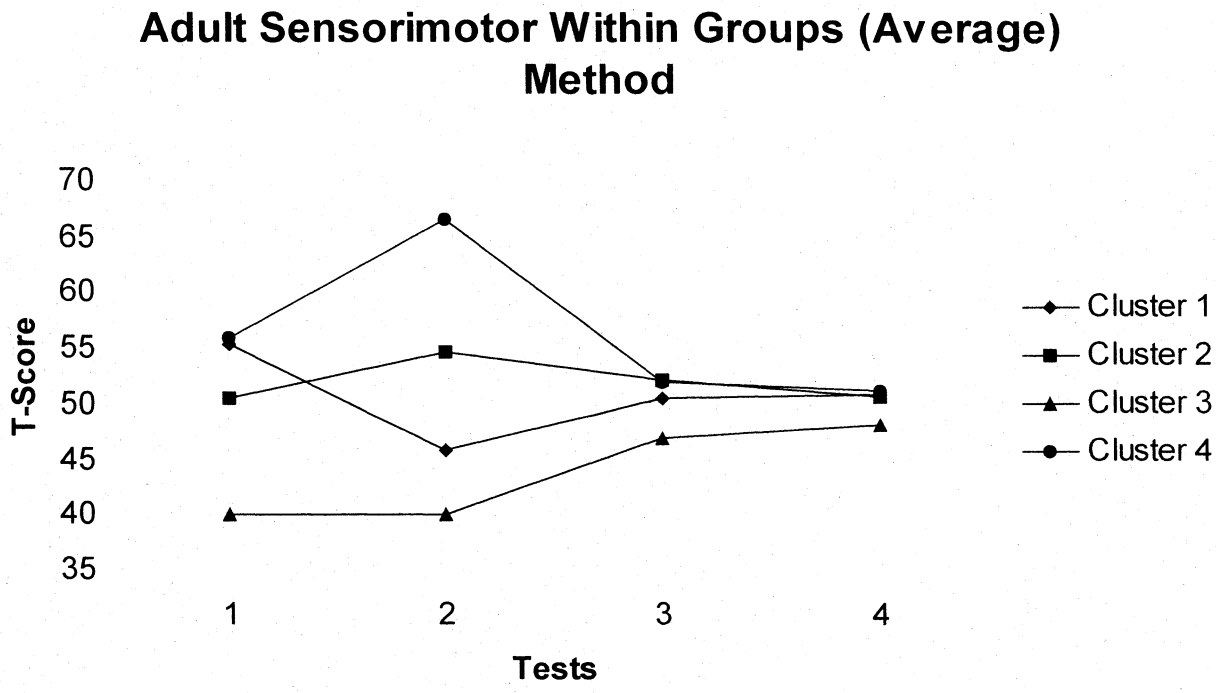

Figure 7. Adult Mean Cluster Values for Within Groups (Average) method, Additional Analyses.

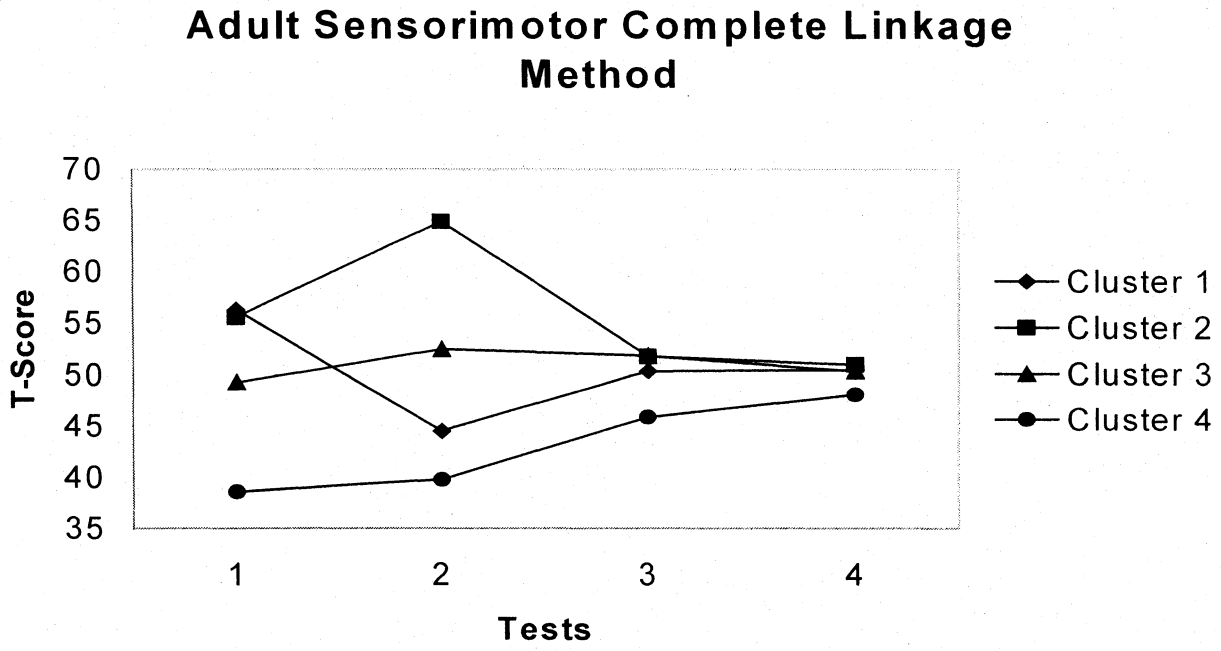

Figure 8. Adult Mean Cluster Values for Complete Linkage Method, Additional Analyses.

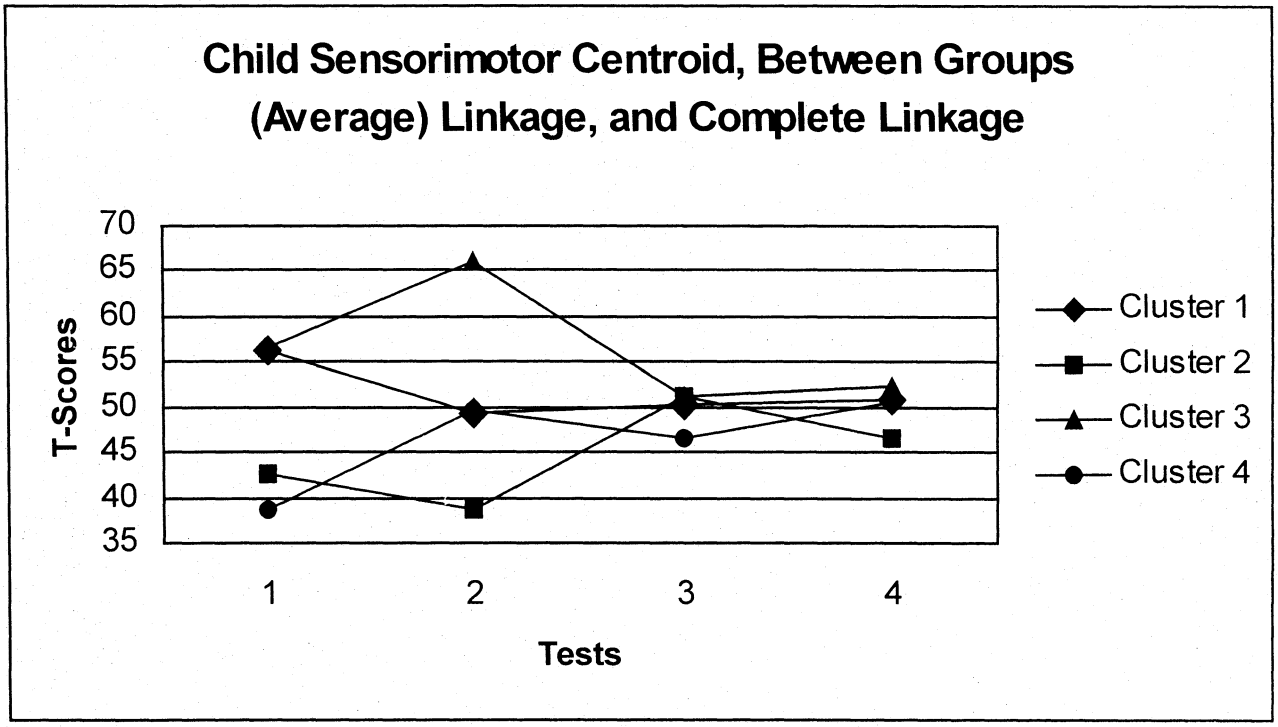

Figure 9. Child Mean Cluster Values for Centroid, Complete Linkage, and Between Groups (Average) Methods, Additional Analyses

simple tactile and gait and station across the solutions. However, Cluster 1 was uniquely characterized by high average finger tapping performance and average grip strength. Cluster 2 was characterized by low average finger tapping performance and below average grip strength. Cluster 3 was characterized by high average finger tapping performance and above average grip strength, and Cluster 4 was characterized by below average finger tapping speed and average grip strength.

To examine the replicability of clusters across the various cluster analytic algorithms for the adult methods, nominal measure of association analyses were conducted. Coefficients of association between the three cluster algorithms employed for adult data is presented in Table 16. All Lambda and Goodman and Kruskal's tau coefficients for the various child solutions had a value of 1.00 for the methods of association analyses and were found to be significant at the $p<.001$ level. Thus, a significant level of association between the cluster solutions generated using the various techniques was obtained for both the child and adult groups. This finding suggests that the four clusters were replicated with good accuracy by Ward's, Within Groups (Average), and Complete Linkage methods for the adult data and by Centroid, Between Groups (Average) linkage, and Complete Linkage for the child groups.

Of particular interest to the current investigation for external validity purposes was the percentage of participants with a diagnosis of depression. Inspection of Table 17 indicated that there were no appreciable differences for depression diagnoses between the clusters for the adult data. The percentage of participants across the clusters provided a close representation of the percentage of participants in the adult

Table 17
Lambda and Goodman and Kruskal's Tau Measurements of Association Between the Three Cluster Analysis Algorithms Utilized For the Adult Sensory Motor Analyses

Method	Ward's		Within Groups (Avg.)		Complete Linkage	
	Lambda	Tau	Lambda	Tau	Lambda	Tau
Ward's	-		.832	.730	.888	.821
Within Groups (Avg.)	.836	.725	-		.940	.895
Complete Linkage	.893	.815	.941	.895	-	

Note. Lambda and Tau values are presented with the methods in the columns as the dependent variable. All values contained in the table were significant at the $p < 0.001$ level.

Table 18
Percent of Depressed and Non Depressed Participants in Each Cluster Across Methods Used for the Adult Data

		%Depressed	%Non-Depressed
Ward's			
n=46	Cluster 1	71	29
n=37	Cluster 2	78	22
n=45	Cluster 3	67	33
n=40	Cluster 4	60	40
Within Groups (Average)			
n=49	Cluster 1	71	29
n=30	Cluster 2	77	33
n=46	Cluster 3	63	37
n=43	Cluster 4	67	33
Complete Linkage			
n=52	Cluster 1	71	29
n=32	Cluster 2	78	22
n=42	Cluster 3	62	38
n=42	Cluster 4	67	33

sample. Analysis of variance for the adult data confirmed there were no differences for percentage of participants that reached at least the $p<0.05$ significance level.

The percentages of children with a diagnosis of depression across the clusters were calculated and are summarized in Table 18. Inspection of the percentage of participants with a diagnosis of depression in the child groups did not indicate any major differences. Analysis of variance was conducted to confirm this finding. Results indicated that there were no significant differences that reached at least the $p<0.05$ significance level.

Thus, the additional cluster analyses that were conducted for the sensorimotor data did not differentiate participants with and without depression for the child and adult groups.

Summary of Results

As anticipated, cluster analyses of the neuropsychological data using a variety of methods yielded reliable and valid cluster solutions for both the child and adult data. The child and adult cluster solutions were characterized by performance level across most subtests of the battery, with a greater division of performance levels present in the adult cluster solutions. Both the child and adult solutions were comprised of clusters that did not differ significantly with respect to a diagnosis of depression. Therefore, the technically valid cluster analyses utilized in the current investigation, conducted on data from a comprehensive neuropsychological evaluation, did not differentiate, in a statistically significant way,

Table 19
Percent of Depressed and Non Depressed Participants in Each Cluster Across Methods Used for the Sensorimotor Child Data

		%Depressed	%Non-Depressed
Complete Linkage Between Groups (Average) Centroid			
n=48	Cluster 1	35	65
n=23	Cluster 2	39	61
n=29	Cluster 3	38	62
n=21	Cluster 4	29	71

participants with and without a diagnosis of depression in both the child and adult groups.

Additional cluster analyses conducted with only sensorimotor data identified cluster solutions that were characterized by unique patterns of finger tapping performance and grip strength. Both child and adult solutions were not comprised of clusters that differed significantly regarding a diagnosis of depression. Thus, the technically valid solutions from the current investigation, conducted on sensorimotor data, also did not differentiate, in a statistically significant way, participants with and without a diagnosis of depression in both the child and adult groups.

Chapter IV: Discussion

The general notion that mental illness is related to brain dysfunction, and that depression represents a unique form of mental illness, provided impetus for the current investigation. Despite longstanding interest in brain-behavior relationships in the discipline of neuropsychology, recent thorough literature reviews provide evidence for a paucity of research, conducted in a systematic manner, examining the complex nature of the brain-behaviour relationships implicated in depression (Veiel, 1997). As a result, a clear conceptualization as to the precise nature of neuropsychological characteristics related to depression, if any, has yet to emerge.

In the neuropsychology clinic, low scores in certain areas of functioning such as motor and processing speed and some executive functions are frequently attributed to depression. This attribution (or quite possibly mis-attribution in some cases) is not evidence-based. At the research level of analysis, it has not yet been clearly established that patterns of data from a comprehensive neuropsychological examination (designed to provide a thorough estimate of brain functioning) can reliably serve as indicators of depression. Prior to the consideration of distinct patterns of neuropsychological functioning, the body of literature in the area of the neuropsychology of depression has yet to provide reliable and valid research results that indicate neuropsychological data can clearly differentiate persons with and without depression. Prior to classification upon distinct patterns, the ability to differentiate is necessary.

The purpose of the current investigation was to utilize statistical clustering methodology to attempt to differentiate groups of participants with and without depression based on data from a comprehensive neuropsychological assessment. This has not been conducted in scientific research in a reliable manner. Results from examination of individual areas of neuropsychological functioning have shown conflicting evidence for specific areas of deficiency in persons with depression. However, results in any one area do not provide adequate information about the relative assets and deficits that would be expected to arise from a thorough neuropsychological evaluation.

To this end, the neuropsychological data were analyzed and three main goals representing three research-based steps to achieve the abovementioned purpose were satisfied.

Goal 1

The first goal was satisfied by applying cluster analytic algorithms to the neuropsychological data of participants with and without depression. These cluster analytic algorithms were applied in separate procedures for the child and adult groups. The cluster analytic methods served to identify solutions that were comprised of differing performance levels across most test results in the neuropsychology battery selected. Similar cluster solutions (i.e., level of performance) had been outlined in cluster analytic studies of a data spanning a wide range of cognitive abilities, such as cluster analytic research investigations of both child and adult Weschler intelligence scales (e.g., Donders 1996; Donders & Warschausky 1997; van

der Heijden & Donders, 2003). Although level of performance, from among the possible outcomes of a cluster analysis, yields less information related to unique patterns of neuropsychological assets and deficits, it has been helpful at the elementary level of analysis when looking to differentiate certain populations and has been shown, in some studies, to be a better predictor of day-to-day outcome variables (e.g., on a academic achievement) than "shape" of cluster profiles (e.g., Watkins & Glutting, 2000). Thus, although detailed discussions of unique cluster profile fluctuations and their implications for complex brain system interactions may not be provided by a cluster solution based upon *level* of performance, for the purposes of the current investigation it provided an opportunity to explore whether this solution reliably differentiated participants with and without a diagnosis of depression. Given the exploratory nature of the current investigation, this was considered to represent a worthwhile and contributory path of exploration at a preliminary level of analysis.

Of particular interest in the present investigation was the question of if in this mixed clinical sample, one that represents a typical sort of patient population in a neuropsychology clinic, one or more levels (e.g., presumably the lowest level(s) of functioning) would be comprised by a significantly greater proportion of participants with depression than when compared to the proportions of participants with depression diagnoses at the other levels of functioning.

In a general sense, in this step of the cluster analytic process, a main goal was to determine if the solutions contained clusters of participants whose test data were more similar to their fellow cluster members than to members of other clusters

(Adams, 1985) and in the current investigation a particular focus on similarity depression diagnosis status was explored. Because cluster analytic methods serve to differentiate groups in most data sets, the differentiation of groups based on the neuropsychological data was successful, as expected, thus satisfying the aforementioned first goal of the current investigation.

Goal 2

In order to proceed with interpretation of the findings it was important to establish that the cluster solutions obtained were not merely a result of the particular clustering algorithms utilized. The cluster solutions for the adult and child groups were replicated with good accuracy in the current investigation, using multiple clustering algorithms. The close and repeated replication of the solutions (i.e., repeatedly providing a similar grouping of participants across the performance levels) allowed conclusions to be attributed to the data.

Specifically, *Goal 2* of the current investigation was satisfied using multiple clustering algorithms and provided evidence for an internally valid solution allowing the final cluster solutions to be interpreted as accurate representations of the data, rather than the clustering techniques utilized.

Goal 3

The third goal of the present investigation was to examine if internally valid solutions represented groups or subgroups that were comprised of significantly different proportions of depressed participants. Statistical analyses designed to compare the proportions of group participants across the child and adult data did not

yield any significant differences across any of the levels. Thus, there was no evidence for a disproportionate amount of cluster members with a diagnosis of depression. Statistical significance was set at a conservative (α=0.05) level, acceptable in most areas of neuropsychological research, particularly given the exploratory nature of the current investigation. Thus, *Goal 3* of the current investigation was satisfied with the aforementioned comparisons for statistical significance. The lack of any appreciable differences, despite this conservative significance level, prevented further justification for additional interpretation of the cluster group differences. Thus, for both the child and adult groups, technically valid solutions failed to differentiate participants with and without diagnoses of depression in this mixed clinical sample based upon the cluster analytic methods utilized for data representing performance on a comprehensive neuropsychological evaluation.

Additional Analyses

The assertion that, for our mixed clinical sample, groups of participants with and without depression could not be statistically differentiated, using cluster analytic methods, was considered with some caution. There are far-reaching implications of these findings that challenge conventional notions pertaining to the neuropsychological sequelae of depression in clinical populations. It was felt that the generalizability of the findings could be enhanced with an additional attempt to differentiate depressed and non-depressed participants.

Thus, there was a need to engage in an attempt at external validation to assist with collection of additional evidence for the assertion that groups of participants with depression could not be differented from groups of participants without depression using cluster analytic methods. Furthermore, given the breadth of the neuropsychological battery in the current investigation, it was possible that either the presence of a number of other test scores unrelated to depression in our sample served to mask the presence of a cluster solution that would allow for this differentiation if fewer test scores were considered.

Selection of the subset of scores for the additional analyses was based on theoretical considerations of the key neuropsychological characteristics thought to be inherent to a depression diagnosis. Given the findings of the current investigation, it was decided to conduct additional analyses on data that are most commonly thought to be affected by depression, namely psychomotor data. The relation of psychomotor functioning to depression is longstanding. As previously mentioned, Kraepelin had implicated voluntary movements as "the most obvious clinical features" of the disease (Kraepelin, 1904).

Data from the sensorimotor battery utilized in the current investigation allowed for further cluster analyses to be conducted in this regard. Of particular importance was to include a reliable measure of motor speed, in addition to assessment of a broad range of motor functions. The Dean-Woodcock Sensory Motor Battery utilized in the current evaluation was viewed as appropriate because of its three underlying factors related to simple sensorimotor, complex sensorimotor, and

subcortical functioning. It was thought that this three-factor structure would allow for ease of discussion pertaining to multiple brain areas affected by brain systems if the cluster solution was successful in differentiating groups of participants with and without diagnoses of depression.

Additional cluster analyses conducted with only sensorimotor data identified cluster solutions that were characterized by differing levels and patterns of finger tapping performance and grip strength. The cluster solutions were demonstrated to be internally valid given the close replication of the solutions in both the child and adult groups. Prior to pattern analyses in the current investigation, it was necessary to first determine if the clusters were characterized by significantly disproportionate representation of participants with and without diagnoses of depression. As was found with the first set of analyses, both child and adult solutions were not comprised by clusters that differed significantly regarding proportion of participants with diagnoses of depression.

Thus, the technically valid solutions from the current investigation, conducted on sensorimotor data also did not differentiate, in a statistically significant way, participants with and without a diagnosis of depression in both the child and adult groups. These additional analyses served to contribute to the generalizability of the results of the current evaluation. This is of particular importance when considering if the breadth of the neuropsychological data utilized in the first set of analyses may have served to interfere with the identification of a valid and reliable cluster solution representative of deficits associated with a diagnosis of depression.

Implications

Attempts at classification and differentiation are fundamental to nearly all aspects of neuropsychology (Morris & Fletcher, 1988). In clinical settings, neuropsychologists are asked to render opinion on the likely effects of specific psychiatric and neurological conditions on neuropsychological functioning. Patients in the neuropsychology clinic are often diagnosed with multiple neuropathological, secondary neurophysiological, and psychiatric disease processes that can affect neuropsychological functioning. As previously mentioned, many of these disease processes place patients at risk for depression. Thus, in clinical settings contemporary neuropsychologists are often asked to render opinion on impaired neuropsychological functioning and complex brain interactions, in addition to the likelihood of impairments in functioning due to various disease processes independent of the effects of depression. It would be helpful for clinical neuropsychologists to develop clear conceptualizations of valid and reliable presentations of depression as evident through a comprehensive neuropsychological examination.

Findings from the present investigation indicated that at the mixed clinical group level utilizing statistical classification analyses, similarity in data variation due to presence or absence of depression diagnosis was not found with the mixed clinical sample and battery utilized. The generalizability of these findings was enhanced when a subsample of the data, selected on conceptually based considerations that motor functioning is likely to be one of the best indicators of depression, also failed to

differentiate participants with and without diagnoses of depression. These findings have implications for consideration of results in clinical settings, particularly when examining neuropsychological test results wherein general functioning appears to be at a lower level and when considering the possible impact of depression on a lower general performance. Certainly, caution must be taken when generalizing to individual cases, and direct parallels should not be drawn between group and case data. However, the results of the current evaluation provide important information to consider when examining the comprehensive neuropsychological test results of patients in a mixed clinical population.

Much of the research-based evidence on differences in specific areas of neuropsycholgical functioning have been conducted on comparisons of depressed persons with normal populations. This framework is not typically one in which clinical neuropsychologists must function when considering a diagnosis of depression. Typically, neuropsychologists must render opinion on expectations on the neuropsychological sequelae of a disease process independent of depression. Thus, results from the current investigation are particularly thought provoking when considering the typical data examined by a clinical neuropsychologist. The results bring into question the sensitivity of the comprehensive neuropsychological examination in identifying changes in functioning due to depression within the context of what would be found in a mixed clinical population.

At the group level of analysis, the results of the current evaluation have implications for providing a context in which to interpret seemingly discrepant research findings.

Of interest to researchers in the area of the neuropsychology of depression is the importance of sample characteristics. As previously mentioned, when compared to normal populations there is a lack of valid and reliable evidence to suggest a pattern of depression. However, individual neuropsychological deficits are sometimes identified. The current evaluation provides a context for consideration of making the distinction between normal and mixed clinical comparisons when conducting research on the neuropsychological characteristics of participants with depression.

One possibility for the lack of differentiation in the current study is the presence of characteristics in the mixed clinical sample that serve to interfere with statistical classification. Specifically, these characteristics could be neuropsychological deficits that are present in depressed participants but also inherent characteristics of multiple disease processes. If present, these characteristics could serve to interfere with differentiation of depressed and non-depressed participants based solely upon neuropsychological data.

As an example, the research of Livingston et al., (1996) examined the performance of children with unipolar depression on the full Halstead-Reitan Neuropsychological Battery for Children and used data from a normative sample as the comparison. In their results, there was no domain or test that fell below one

standard deviation below the mean in comparison to normative data for children diagnosed with depression. However, the lowest area of performance, a Freedom From Distractability composite, fell between 0.9 and 1 standard deviations below the mean. If in a mixed clinical sample of children, there are a large number of conditions that could interfere with freedom from distractibility (e.g., ADHD), and if the findings are statistically subtle when compared to normative data, then as was found in the current investigation, they may not be detected in research with mixed clinical populations.

Thus, results from the current investigation provide important methodological and interpretative considerations from a research-based perspective.

Limitations

There are a number of possible limitations to the current investigation that must be considered. First, as mentioned previously, are the possible limitations posed by sample characteristics. The depression diagnoses were defined based upon a DSM-IV diagnosis of depression. This diagnosis was not further classified in terms of severity of depression, stage, medication status, or other depression characteristics. This decision was made based on aforementioned findings that indicated exclusion of patients with psychosis or bipolar disorder were the most salient sample criteria to consider for participants with depression. Thus, there were a number of other possible sample characteristics that could have been controlled. Furhtermore, results may have differed had participants been requested to rate the severity of their depression. Participant self-rating was avoided because results from previous

investigations indicated that self-ratings of depressive symptoms could be overestimated by participants (e.g., Rohling, Green, Allen, & Iverson 2002). Thus, there was no practical way, given the scope of the data included in the current evaluation, to accurately account for severity of depression aside from inpatient versus outpatient status. As a result, conclusions of the current evaluation are limited to the outpatient mixed clinical populations. Furthermore, interpretation of studies indicating significant deficits for inpatient participants with depression (e.g., Burt, Zembar, & Niederehe, 1995) are limited with respect to their relevance to the findings of the current evaluation.

It was also decided not to distinguish among medicated and non-medicated participants as this information was not readily available and because previous research (e.g., Boone et al., 1995) had indicated that this would not be necessary in a mixed clinical sample. Again, this posed a limitation to the interpretation of the results of the current investigation as an absence of context for information related to neuropsychological functioning and medication status in participants with depression.

Other sample characteristics, such as inclusion of participants at different phases of their illness, are suggested by some researchers as plausible explanations for an absence of significant findings. Merriam et al. (1999) assert that given the convergence of executive deficits with neuroimaging studies indicating resting-state and activation deficits in persons with depression, it is surprising that studies of neuropsychological functioning do not support clear deficiencies in executive functioning for these persons. However, the principal task in the current investigation

was conducted to determine if data from a comprehensive neuropsychological battery would reliably and significantly differentiate participants from a mixed clinical sample. Thus, an absence of significantly different groups in this regard does not necessarily imply that individual differences in neuropsychological functioning for participants with and without depression diagnoses would not be found if tested independently. Indeed, given the review of research in the area there may likely be significant differences. These differences may not be the same for child and adult groups. Nonetheless, by not conducting these sorts of analyses, limitations are posed for speaking about isolated deficits and directly contributing to information on individual brain areas such as are currently being conducted with neuroimaging studies.

Future Research

Scientists conducting future research investigations designed to replicate the current investigation may benefit from the opportunity to examine the methodology utilized. Although two technically valid and reliable solutions were produced for the main and additional cluster analyses, there may be alternate avenues worthy of exploration in cluster analytic methodology. For example, Squared Euclidean distance was utilized as the distance measure in the current evaluation. Although well respected for its use in research with neuropsychological data, Squared Euclidean Distance is considered as a distance measure that is strongly sensitive to level of clusters. A worthwhile follow-up investigation would appear to involve selecting a distance measure less sensitive to level that may allow for a wider range of solutions

with varying patterns to possibly arise. Furthermore, alternate methods designed to replicate the cluster solutions may also be worthwhile exploring. Given a large enough sample size, running the cluster analyses independently on half of the sample is an alternate method for testing the reliability of the solutions. An increase in sample size would also be desirable because of the large number of variables required when attempting to represent data from a comprehensive neuropsychological evaluation in cluster analytic methodology.

It appears reasonable to consider that one primary goal of these aforementioned alternate methodological considerations would be to identify cluster solutions that were not generated using the methodology of the current investigation (despite having examined many possible solutions in great detail).

Another goal would be to provide replication and confidence in the reliability and validity of the analyses conducted in the present investigation.

Results from replication studies of the current investigation will likely yield clarification on the aforementioned issues related to research limitations such as depression severity, medication status, and comorbid functioning will have a stronger foundation upon which to build. Once information is gleaned as to the effects of these various characteristics on studying groups of participants with depression, it is hoped that further research investigations will be conducted that provide greater insight into the brain-behavior basis of depression useful for both research and clinical settings.

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